

utility of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, known, etc. known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Borrelidin-producing polyketide synthase & the use

Inventors (please provide full names):

Salas J A et al.

Earliest Priority Filing Date 12/27/2002

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

please search formula I and formula 2
in claim 75 (see attached)

(a) In formula I



$R_5, R_{10} = OH$

$R_4 = CH_3, COOH, CN$

Other R - leave open

(b) in formula 2

$R_4, R_{10} = OH$

$R_4 = CH_3, COOH, CN$

Other R - leave
open

10/534210

***** INVENTOR RESULTS *****

=> d his l42

(FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 09:00:06 ON 04 SEP 2008)
SAVE TEMP L41 KAM240MULTIN/A

FILE 'HCAPLUS' ENTERED AT 09:04:34 ON 04 SEP 2008

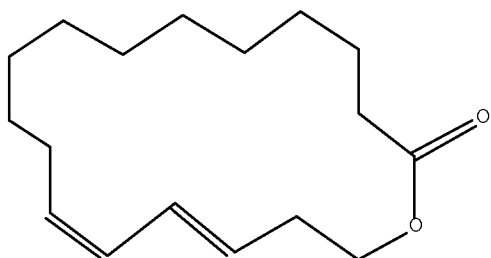
L42 7 S ((L22-L31) AND L10) OR (L1 AND L10)

=> d que l42

L1 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US20070065920/PN

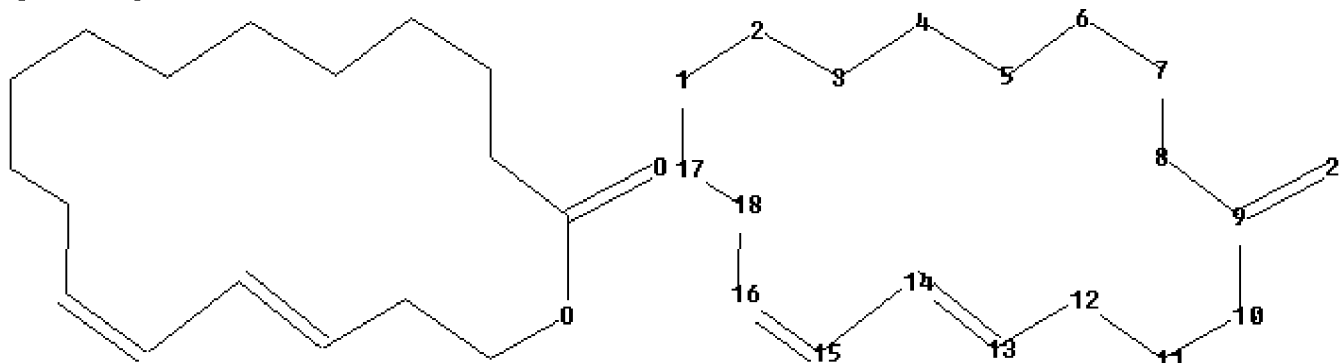
L2 SCR 2043 OR 1918

L3 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



chain nodes :

20

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

chain bonds :

9-20

ring bonds :

1-2 1-17 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-12 12-13 13-14 14-15

15-16 16-18 17-18

exact/norm bonds :

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exact bonds :

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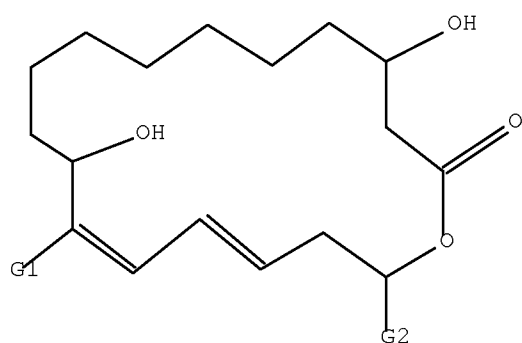
10/534210

15
15-16 16-18 17-18
isolated ring systems :
containing 1 :

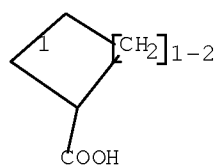
Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 20:CLASS

L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2
L6 STR



G1 Me,COOH,CN
G2 [C1],[C2],[C3]

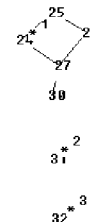
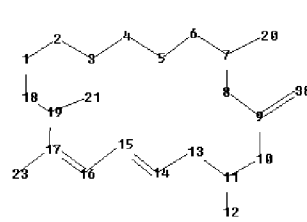
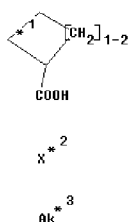
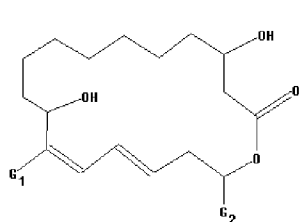


X²

Ak³

Structure attributes must be viewed using STN Express query preparation:

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chain nodes :
12 20 21 23 30 31 32 38
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 13 14 15 16 17 18 19 24 25 26 27
chain bonds :
7-20 9-38 11-12 17-23 19-21 27-30
ring bonds :

10/534210

1-2 1-18 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-13 13-14 14-15 15-16
16-17 17-19 18-19 24-25 24-27 25-26 26-27
exact/norm bonds :
7-20 9-38 11-12 17-23 19-21
exact bonds :
1-2 1-18 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-13 13-14 14-15 15-16
16-17 17-19 18-19 24-25 24-27 25-26 26-27 27-30
isolated ring systems :
containing 1 : 24 :

G1:CH3,COOH,CN

G2:[*1],[*2],[*3]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:CLASS 21:CLASS
23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom 30:CLASS 31:CLASS 32:CLASS
38:CLASS

L9 17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L10 86 SEA FILE=HCAPLUS ABB=ON PLU=ON L9
L22 478 SEA FILE=HCAPLUS ABB=ON PLU=ON SALAS J?/AU
L23 305 SEA FILE=HCAPLUS ABB=ON PLU=ON MENDEZ C?/AU
L24 51 SEA FILE=HCAPLUS ABB=ON PLU=ON OLANO C?/AU
L25 3325 SEA FILE=HCAPLUS ABB=ON PLU=ON SANCHEZ C?/AU
L26 100 SEA FILE=HCAPLUS ABB=ON PLU=ON BRANA A?/AU
L27 449 SEA FILE=HCAPLUS ABB=ON PLU=ON WILKINSON B?/AU
L28 5002 SEA FILE=HCAPLUS ABB=ON PLU=ON MARTIN C?/AU
L29 1074 SEA FILE=HCAPLUS ABB=ON PLU=ON MOSS S?/AU
L30 197 SEA FILE=HCAPLUS ABB=ON PLU=ON LEADLAY P?/AU
L31 16 SEA FILE=HCAPLUS ABB=ON PLU=ON OLIYNYK M?/AU
L42 7 SEA FILE=HCAPLUS ABB=ON PLU=ON (((L22 OR L23 OR L24 OR L25
OR L26 OR L27 OR L28 OR L29 OR L30 OR L31)) AND L10) OR (L1
AND L10)

=> d his 141

(FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 09:00:06 ON 04 SEP 2008)
L41 6 S L40 AND BORRELIDIN

=> d que 141

L22 478 SEA FILE=HCAPLUS ABB=ON PLU=ON SALAS J?/AU
L23 305 SEA FILE=HCAPLUS ABB=ON PLU=ON MENDEZ C?/AU
L24 51 SEA FILE=HCAPLUS ABB=ON PLU=ON OLANO C?/AU
L25 3325 SEA FILE=HCAPLUS ABB=ON PLU=ON SANCHEZ C?/AU
L26 100 SEA FILE=HCAPLUS ABB=ON PLU=ON BRANA A?/AU
L27 449 SEA FILE=HCAPLUS ABB=ON PLU=ON WILKINSON B?/AU
L28 5002 SEA FILE=HCAPLUS ABB=ON PLU=ON MARTIN C?/AU
L29 1074 SEA FILE=HCAPLUS ABB=ON PLU=ON MOSS S?/AU
L30 197 SEA FILE=HCAPLUS ABB=ON PLU=ON LEADLAY P?/AU
L31 16 SEA FILE=HCAPLUS ABB=ON PLU=ON OLIYNYK M?/AU

10/534210

L40 176 SEA ((L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
L30 OR L31)) AND BIOSYNTHET? GENE#
L41 6 SEA L40 AND BORRELIDIN

=> dup rem l42 l41

FILE 'HCAPLUS' ENTERED AT 09:10:22 ON 04 SEP 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 09:10:22 ON 04 SEP 2008

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Copyright (c) 2008 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 09:10:22 ON 04 SEP 2008
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PROCESSING COMPLETED FOR L42
PROCESSING COMPLETED FOR L41

L44 8 DUP REM L42 L41 (5 DUPLICATES REMOVED)
ANSWERS '1-7' FROM FILE HCAPLUS
ANSWER '8' FROM FILE BIOSIS

=> d l44 1-7 ibib abs hitstr; d l44 8 ibib ab

L44 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:547408 HCAPLUS Full-text
DOCUMENT NUMBER: 141:202986
TITLE: Biosynthesis of the angiogenesis inhibitor borrelidin
by Streptomyces parvulus Tue4055: Insights into
nitrile formation
AUTHOR(S): Olano, Carlos; Moss, Steven J.;
Brana, Alfredo F.; Sheridan, Rose M.; Math,
Vidya; Weston, Alison J.; Mendez, Carmen;
Leadlay, Peter F.; Wilkinson, Barrie
; Salas, Jose A.
CORPORATE SOURCE: Departamento de Biologia Funcional e Instituto
Universitario de Oncologia del Principado de Asturias
(IUOPA), Universidad de Oviedo, Oviedo, 33006, Spain
SOURCE: Molecular Microbiology (2004), 52(6), 1745-1756
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 18-membered polyketide macrolide borrelidin exhibits a number of important
biol. activities, including potent angiogenesis inhibition. This has prompted
two recent total syntheses as well as the cloning of the biosynthetic gene
cluster from Streptomyces parvulus Tue4055. Borrelidin possesses some unusual
structural characteristics, including a cyclopentane carboxylic acid moiety at
C17 and a nitrile moiety at C12 of the macrocyclic ring. Nitrile groups are
relatively rare in nature, and little is known of their biosynthesis during
secondary metabolism. The nitrile group of borrelidin is shown here to arise
from the Me group of a methylmalonyl-CoA extender unit incorporated during
polyketide chain extension. Insertional inactivation of two genes in the
borrelidin gene cluster, borI (coding for a cytochrome P 450 monooxygenase)
and borJ (coding for an aminotransferase), generated borrelidin non-producing
mutants. These mutants accumulated different compds. lacking the C12 nitrile
moiety, with the product of the borI-minus mutant (12-desnitrile-12-methyl-
borrelidin) possessing a Me group and that of the borJ-minus mutant (12-

desnitrile-12-carboxyl-borrelidin) a carboxyl group at C12. The former but not the latter was converted into borrelidin when biotransformed by an *S. parvulus* mutant that is deficient in the biosynthesis of the borrelidin starter unit. This suggests that 12-desnitrile-12-methyl-borrelidin is a competent biosynthetic intermediate, whereas the carboxylated derivative is a shunt metabolite. Bioconversion of 12-desnitrile-12-methyl-borrelidin into borrelidin was also achieved in a heterologous system co-expressing *borI* and *borJ* in *Streptomyces albus* J1074. This bioconversion was more efficient when *borK*, which is believed to encode a dehydrogenase, was simultaneously expressed with *borI* and *borJ*. On the basis of these findings, a pathway is proposed for the formation of the nitrile moiety during borrelidin biosynthesis.

IT 7184-60-3, Borrelidin

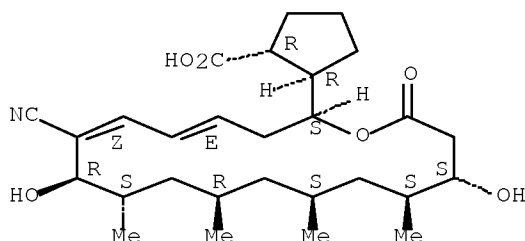
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biosynthesis of angiogenesis inhibitor borrelidin by *Streptomyces parvulus* Tue4055 and formation of nitrile moiety)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:96852 HCAPLUS Full-text

DOCUMENT NUMBER: 141:48175

TITLE: Biosynthesis of the Angiogenesis Inhibitor Borrelidin by *Streptomyces parvulus* Tu4055. Cluster Analysis and Assignment of Functions

AUTHOR(S): Olano, Carlos; Wilkinson, Barrie;
Sanchez, Cesar; Moss, Steven J.;
Sheridan, Rose; Math, Vidya; Weston, Alison J.;
Brana, Alfredo F.; Martin, Christine
J.; Oliynyk, Markiyan; Mendez,
Carmen; Leadlay, Peter F.; Salas,
Jose A.

CORPORATE SOURCE: Departamento de Biologia Funcional e Instituto
Universitario de Oncologia del Principado de Asturias,
Universidad de Oviedo, Oviedo, 33006, Spain

SOURCE: Chemistry & Biology (2004), 11(1), 87-97

CODEN: CBOLE2; ISSN: 1074-5521

PUBLISHER: Cell Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The biosynthetic gene cluster for the angiogenesis inhibitor borrelidin has been cloned from *Streptomyces parvulus* Tu4055. Sequence anal. indicates that the macrolide ring of borrelidin is formed by a modular polyketide synthase (PKS) (borA1-A6), a result that was confirmed by disruption of borA3. The borrelidin PKS is striking because only seven rather than the nine modules expected for a nonaketide product are encoded by borA1-A6. The starter unit of the PKS has been verified as trans-cyclopentane-1,2-dicarboxylic acid (trans-1,2-CPDA), and the genes involved in its biosynthesis identified. Other genes responsible for biosynthesis of the nitrile moiety, regulation, and self-resistance were also identified.

IT 7184-60-3, Borrelidin

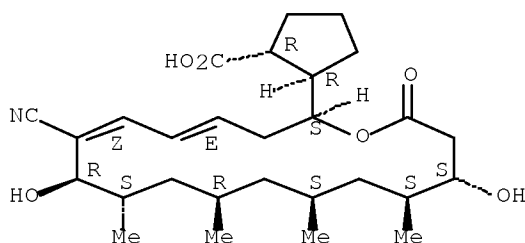
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequence of borrelidin biosynthetic gene cluster of *Streptomyces parvulus* Tu4055)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1364394 HCAPLUS Full-text

DOCUMENT NUMBER: 148:11000

TITLE: Preparation of borrelidin derivatives as anticancer agents

INVENTOR(S): Wilkinson, Barrie; Moss, Steven; Zhang, Ming

PATENT ASSIGNEE(S): Biotica Technology Limited, UK

SOURCE: PCT Int. Appl., 48pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007135078	A2	20071129	WO 2007-EP54801	20070517
WO 2007135078	A3	20080221		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,

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GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK,
MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.:

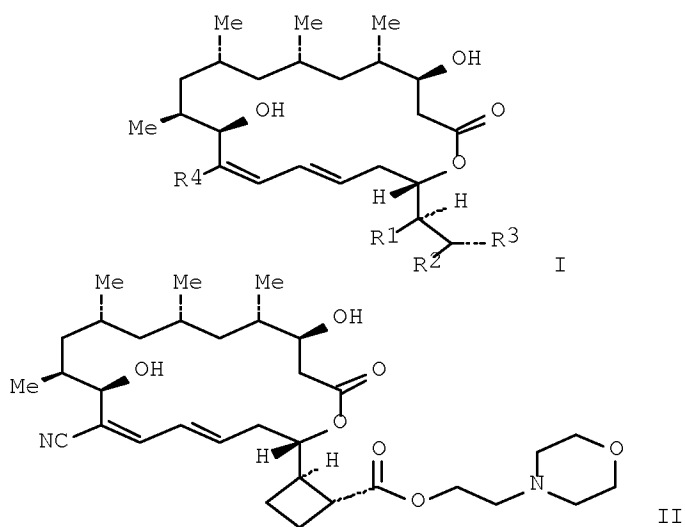
GB 2006-9981

A 20060519

OTHER SOURCE(S):

CASREACT 148:11000; MARPAT 148:11000

GI



AB Borrelidin derivs. of formula I [R1, R2 = H, alkyl, etc.; R1R2 = CH2CH2, etc.; R3 = CONHR5, CO2R5, etc.; R4 = CN, CO2H, Me, CONH2; R5 = H, (substituted) alkyl, etc.] are prepared for the treatment of cancer or B-cell malignancies, or other diseases in which angiogenesis contributes to the pathol., including ophthalmic disorders such as diabetic retinopathy as well as age related macular degeneration (AMD), corneal neovascularization and retinopathy or prematurity. The present invention also provides methods for the production of these compds. and their use in medicine, in particular in the treatment and/or prophylaxis of cancer or B-cell malignancies and other diseases in which angiogenesis is implicated in the pathogenic process. Thus, II is prepared, and had 0.84 ratio of inhibition of CAM vasculature at 25 ng/CAM to in vitro cancer cell inhibition at 1 μ M.

IT 724426-07-7P

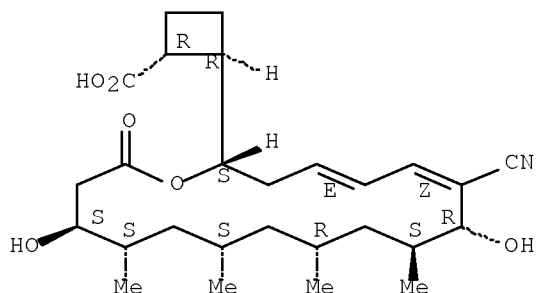
RL: PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of borrelidin derivs. as anticancer agents)

RN 724426-07-7 HCAPLUS

CN Cyclobutanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-

yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L44 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1048524 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 146:38421

TITLE: Separation of anti-angiogenic and cytotoxic activities of borrelidin by modification at the C17 side chain

AUTHOR(S): Wilkinson, Barrie; Gregory, Matthew A.;
Moss, Steven J.; Carletti, Isabelle; Sheridan,
Rose M.; Kaja, Andrew; Ward, Michael; Olano,
Carlos; Mendez, Carmen; Salas,
Jose A.; Leadlay, Peter F.; van
Ginckel, Rob; Zhang, Ming-Qiang

CORPORATE SOURCE: Biotica Technology Ltd., Little Chesterford, Essex,
CB10 1XL, UK

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006),
16(22), 5814-5817

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A set of novel borrelidin analogs have been prepared by precursor-directed biosynthesis. Structure-activity relationship anal. suggests that steric structural arrangement within the C17 side chain is important for differentiating cytotoxic and antiangiogenic activities. A C17-cyclobutyl analog 3 was found to have markedly increased selectivity for in vitro angiogenesis inhibition over cytotoxicity and is therefore potentially useful as an anticancer agent.

IT 7184-60-3, Borrelidin 724426-05-5 724426-07-7
901327-48-8 901327-52-4 901327-55-7
901327-63-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(separation of anti-angiogenic and cytotoxic activities of borrelidin by modification at the C17 side chain)

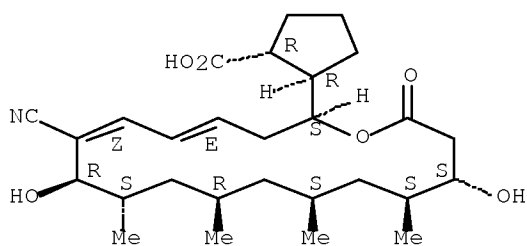
RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

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Double bond geometry as shown.

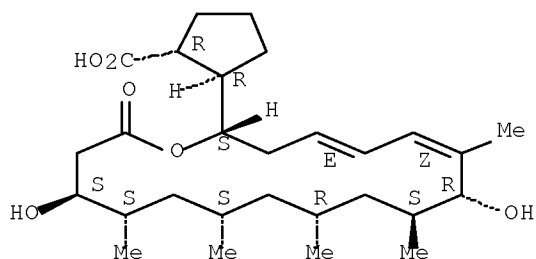


RN 724426-05-5 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-8,16-dihydroxy-7,9,11,13,15-pentamethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

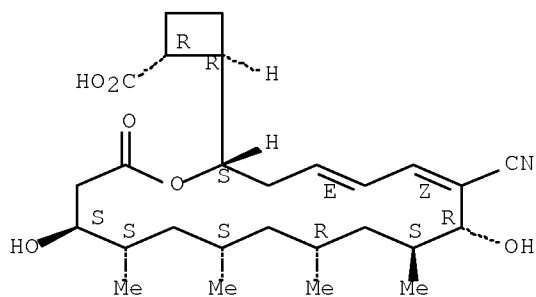


RN 724426-07-7 HCAPLUS

CN Cyclobutanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

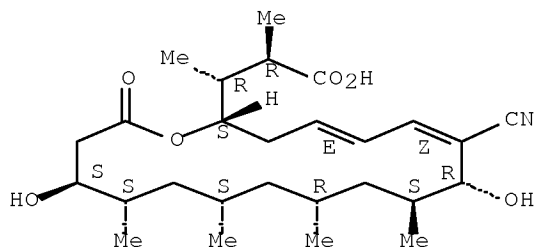


RN 901327-48-8 HCAPLUS

10/534210

CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-
 $\alpha, \beta, 9, 11, 13, 15$ -hexamethyl-18-oxo-,
 $(\alpha R, \beta R, 2S, 4E, 6Z, 8R, 9S, 11R, 13S, 15S, 16S)$ - (CA INDEX NAME)

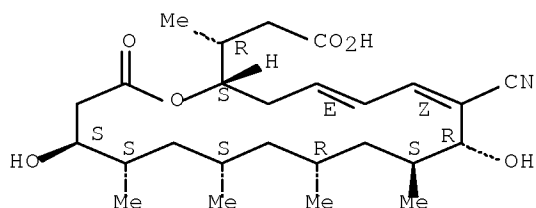
Absolute stereochemistry.
 Double bond geometry as shown.



RN 901327-52-4 HCAPLUS

CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-
 $\beta, 9, 11, 13, 15$ -pentamethyl-18-oxo-, $(\beta R, 2S, 4E, 6Z, 8R, 9S, 11R, 13S, 15S, 16S)$ - (CA INDEX NAME)

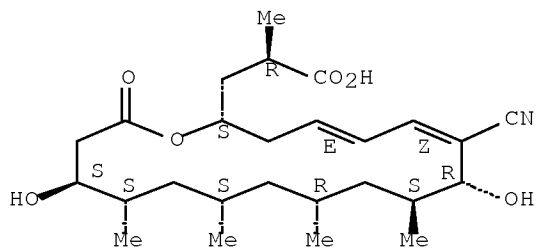
Absolute stereochemistry.
 Double bond geometry as shown.



RN 901327-55-7 HCAPLUS

CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-
 $\alpha, 9, 11, 13, 15$ -pentamethyl-18-oxo-, $(\alpha R, 2S, 4E, 6Z, 8R, 9S, 11R, 13S, 15S, 16S)$ - (CA INDEX NAME)

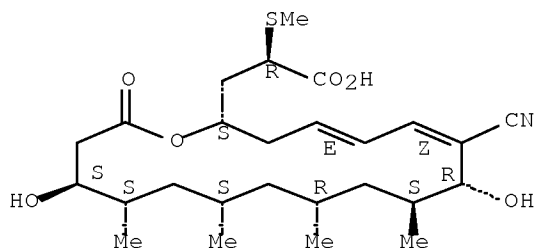
Absolute stereochemistry.
 Double bond geometry as shown.



10/534210

RN 901327-63-7 HCAPLUS
CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-
9,11,13,15-tetramethyl- α -(methylthio)-18-oxo-,
(α R,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

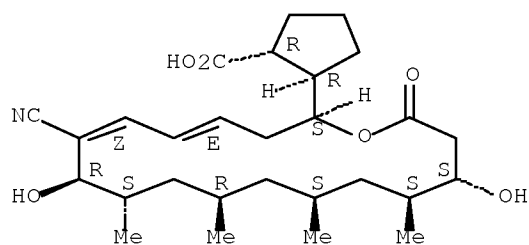
Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

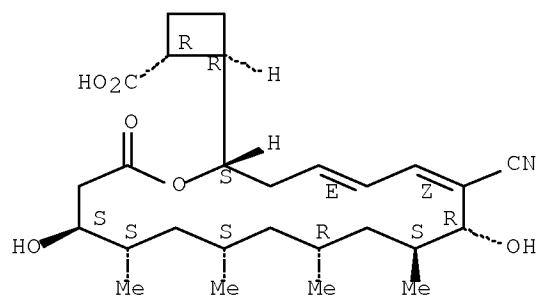
L44 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:507221 HCAPLUS Full-text
DOCUMENT NUMBER: 145:165577
TITLE: Biosynthesis of the angiogenesis inhibitor borrelidin:
directed biosynthesis of novel analogues
AUTHOR(S): Moss, Steven J.; Carletti, Isabelle;
Olano, Carlos; Sheridan, Rose M.; Ward,
Michael; Math, Vidya; Nur-E-Alam, Mohammad;
Brana, Alfredo F.; Zhang, Ming Qiang;
Leadlay, Peter F.; Mendez, Carmen;
Salas, Jose A.; Wilkinson, Barrie
CORPORATE SOURCE: Biotica, Little Chesterford, CB10 1XL, UK
SOURCE: Chemical Communications (Cambridge, United Kingdom)
(2006), (22), 2341-2343
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:165577
AB We report the directed biosynthesis of borrelidin analogs and their selective
anti-proliferative activity against human cancer cell lines.
IT 7184-60-3F, Borrelidin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP
(Preparation)
(directed biosynthesis of novel borrelidin analogs)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-
8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-
yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



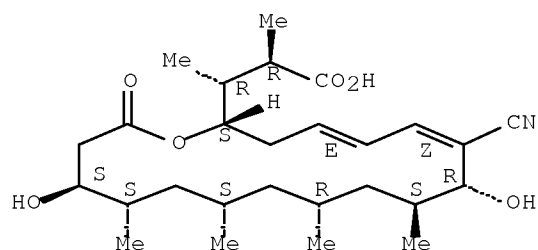
IT 724426-07-7P 901327-48-8P 901327-52-4P
 901327-55-7P 901327-59-1P 901327-63-7P
 RL: BMF (Bioindustrial manufacture); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
 (directed biosynthesis of novel borrelidin analogs)
 RN 724426-07-7 HCAPLUS
 CN Cyclobutanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxoxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 901327-48-8 HCAPLUS
 CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy- α,β ,9,11,13,15-hexamethyl-18-oxo-,
 (α R, β R,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

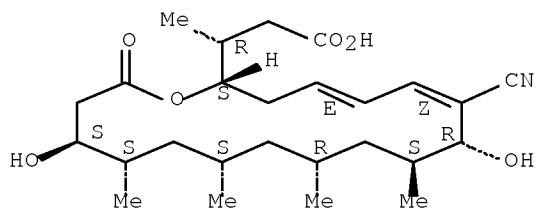


RN 901327-52-4 HCAPLUS

CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-
 β ,9,11,13,15-pentamethyl-18-oxo-, (β R,2S,4E,6Z,8R,9S,11R,13S,15S,
 16S)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

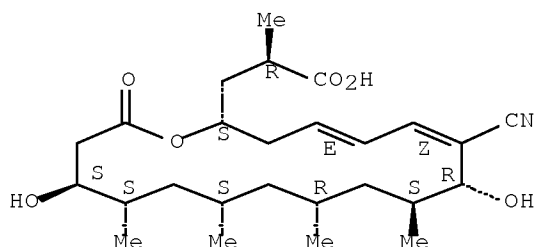


RN 901327-55-7 HCAPLUS

CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-
 α ,9,11,13,15-pentamethyl-18-oxo-, (α R,2S,4E,6Z,8R,9S,11R,13S,1
 5S,16S)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

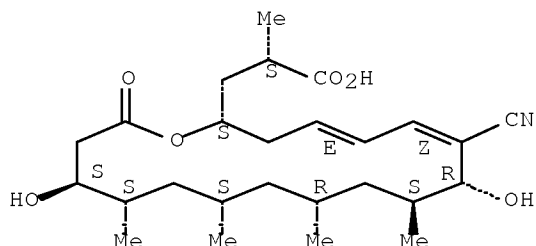


RN 901327-59-1 HCAPLUS

CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-
 α ,9,11,13,15-pentamethyl-18-oxo-, (α S,2S,4E,6Z,8R,9S,11R,13S,1
 5S,16S)- (CA INDEX NAME)

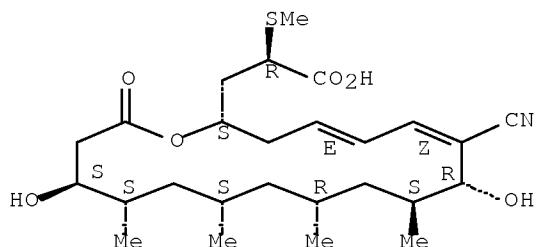
Absolute stereochemistry.

Double bond geometry as shown.



RN 901327-63-7 HCAPLUS
 CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-
 9,11,13,15-tetramethyl- α -(methylthio)-18-oxo-,
 (α R,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:570032 HCAPLUS Full-text
 DOCUMENT NUMBER: 141:118341
 TITLE: The borrelidin biosynthetic gene cluster of Streptomyces parvulus Tu4055 and its use in the development of novel polyketide with therapeutic uses
 INVENTOR(S): Salas, Jose A.; Mendez, Carmen; Olano, Carlos; Sanchez, Cesar; Brana, Alfredo F.; Wilkinson, Barrie; Martin, Christine J.; Moss, Steven; Leadlay, Peter F.; Oliynyk, Marko
 PATENT ASSIGNEE(S): Biotica Technology Limited, UK; The University of Oviedo
 SOURCE: PCT Int. Appl., 255 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058976	A2	20040715	WO 2003-GB5704	20031224
WO 2004058976	A3	20050217		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

10/534210

CA 2506669	A1	20040715	CA 2003-2506669	20031224
AU 2003295169	A1	20040722	AU 2003-295169	20031224
EP 1576160	A2	20050921	EP 2003-786170	20031224
EP 1576160	B1	20070502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017118	A	20051025	BR 2003-17118	20031224
CN 1732264	A	20060208	CN 2003-80107717	20031224
JP 2006514548	T	20060511	JP 2004-563382	20031224
AT 361286	T	20070515	AT 2003-786170	20031224
EP 1840216	A2	20071003	EP 2007-107182	20031224
EP 1840216	A3	20071017		
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ES 2287552	T3	20071216	ES 2003-786170	20031224
EP 1961747	A2	20080827	EP 2007-106112	20031224
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IN 2005KN00733	A	20060324	IN 2005-KN733	20050426
MX 2005PA05323	A	20060310	MX 2005-PA5323	20050518
US 20070065920	A1	20070322	US 2006-534210	20060317 <--
IN 2007KN01744	A	20080801	IN 2007-KN1744	20070516
IN 2007KN01745	A	20080801	IN 2007-KN1745	20070516
PRIORITY APPLN. INFO.:			GB 2002-30217	A 20021227
			EP 2003-786170	A3 20031224
			WO 2003-GB5704	W 20031224
			IN 2005-KN733	A3 20050426

OTHER SOURCE(S): MARPAT 141:118341

AB The biosynthetic gene cluster for the angiogenesis inhibitor borrelidin of *Streptomyces parvulus* Tu4055 is cloned and characterized. The coding regions for the individual domains of the enzyme may be used in the development of novel polyketide synthases for the manufacture of novel polyketides including borrelidin and analogs and derivs. The macrolide ring of borrelidin is formed by a modular polyketide synthase (PKS) encoded by six open reading frames (borA1-A6), a result that was confirmed by disruption of the borA3 open reading frame. The borrelidin PKS is striking because only seven rather than the nine modules expected for a nonaketide product are encoded by borA1-A6. The starter unit of the PKS has been verified as trans-cyclopentane-1,2-dicarboxylic acid (trans-1,2-CPDA), and the genes involved in its biosynthesis identified. Cloning of the genes by expression in *Escherichia coli* is described. Other genes responsible for biosynthesis of the nitrile moiety, regulation, and self-resistance are also identified.

IT 196869-69-9 724426-05-5 724426-06-6
724426-07-7

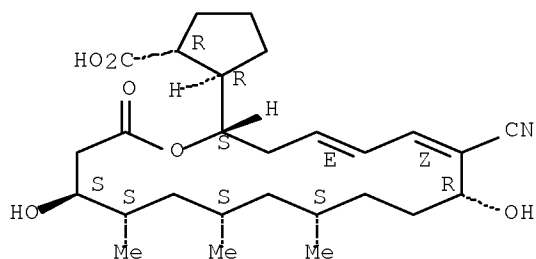
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biosynthesis of, with engineered borrelidin synthase; borrelidin biosynthetic gene cluster of *Streptomyces parvulus* Tu4055 and its use in development of novel polyketide with therapeutic uses)

RN 196869-69-9 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,11S,13S,15S,16S)-7-cyano-8,16-dihydroxy-11,13,15-trimethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

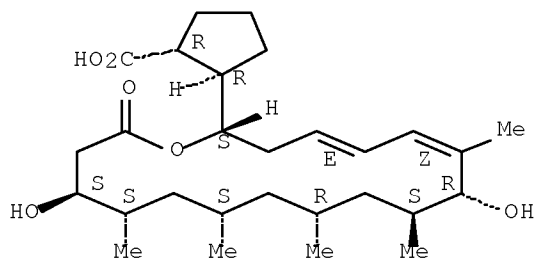
Double bond geometry as shown.



RN 724426-05-5 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-8,16-dihydroxy-7,9,11,13,15-pentamethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

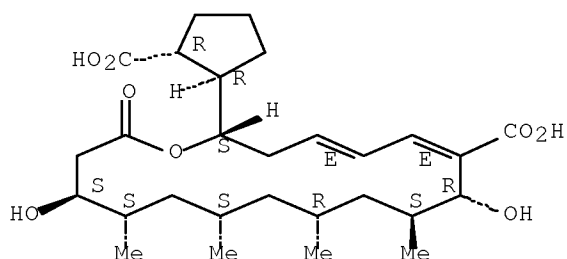
Absolute stereochemistry.
Double bond geometry as shown.



RN 724426-06-6 HCAPLUS

CN Oxacyclooctadeca-4,6-diene-7-carboxylic acid, 2-[(1R,2R)-2-carboxycyclopentyl]-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxo-, (2S,4E,6E,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

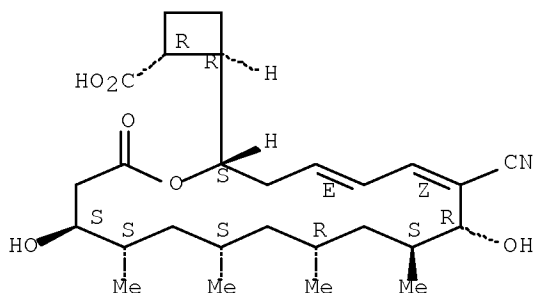


RN 724426-07-7 HCAPLUS

CN Cyclobutanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-

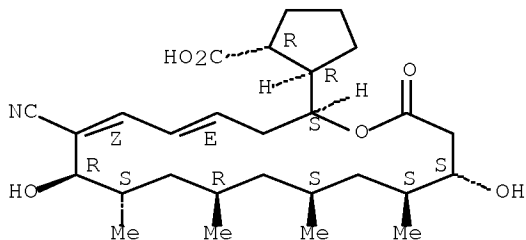
yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 7184-60-3P, Borrelidin
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 BIOL (Biological study); PREP (Preparation)
 (gene cluster for biosynthesis of; borrelidin biosynthetic gene cluster
 of *Streptomyces parvulus* Tu4055 and its use in development of novel
 polyketide with therapeutic uses)
 RN 7184-60-3 HCAPLUS
 CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-
 8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-
 yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

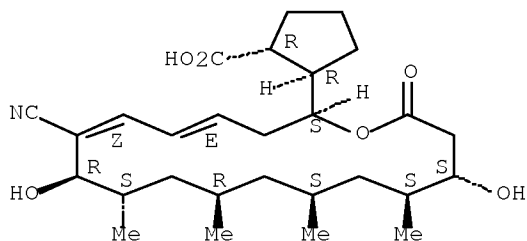


L44 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:857652 HCAPLUS [Full-text](#)
 DOCUMENT NUMBER: 140:195301
 TITLE: Evidence from engineered gene fusions for the repeated
 use of a module in a modular polyketide synthase
 AUTHOR(S): Olano, Carlos; Wilkinson, Barrie;
 Moss, Steven J.; Brana, Alfredo F.;
 Mendez, Carmen; Leadlay, Peter F.;
 Salas, Jose A.
 CORPORATE SOURCE: Departamento de Biologia Funcional e Instituto
 Universitario de Oncologia del Principado de Asturias
 (I.U.O.P.A), Universidad de Oviedo, Oviedo, 33006,
 Spain

10/534210

SOURCE: Chemical Communications (Cambridge, United Kingdom)
(2003), (22), 2780-2782
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Functional evidence for programmed loss of co-linearity on the borrelidin
modular polyketide synthase (PKS) is presented.
IT 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(evidence from engineered gene fusions for repeated use of a module in
borrelidin modular polyketide synthase)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-
8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-
yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:589076 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600599702
TITLE: Potent angiogenesis inhibitors derived from
borrelidin: SAR and antitumor activities.
AUTHOR(S): Wilkinson, Barrie [Reprint Author]; Moss,
Steven J.; Carletti, Isabelle; Vousden, William;
Coates, Nigel; Olano, Carlos; Sheridan, Rose M.;
Mendez, Carmen; Salas, Jose A.;
Leadlay, Peter F.; Zhang, Ming-Qiang
CORPORATE SOURCE: Univ Oviedo, Dept Biol Funct, Oviedo, Spain
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (APR 2006) Vol. 47, pp. 1344.
Meeting Info.: 97th Annual Meeting of the
American-Association-for-Cancer-Research (AACR).
Washington, DC, USA. April 01 -05, 2006. Amer Assoc Canc
Res.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Nov 2006
Last Updated on STN: 8 Nov 2006

10/534210

***** QUERY RESULTS *****

=> d his l43

(FILE 'HCAPLUS' ENTERED AT 09:04:34 ON 04 SEP 2008)

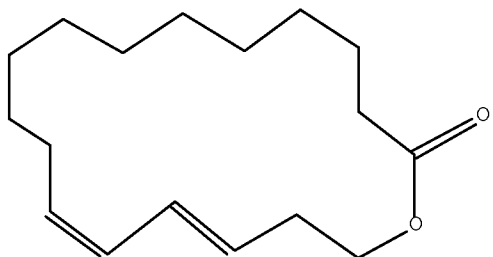
L43 30 S L21 NOT L42

=> d que l43

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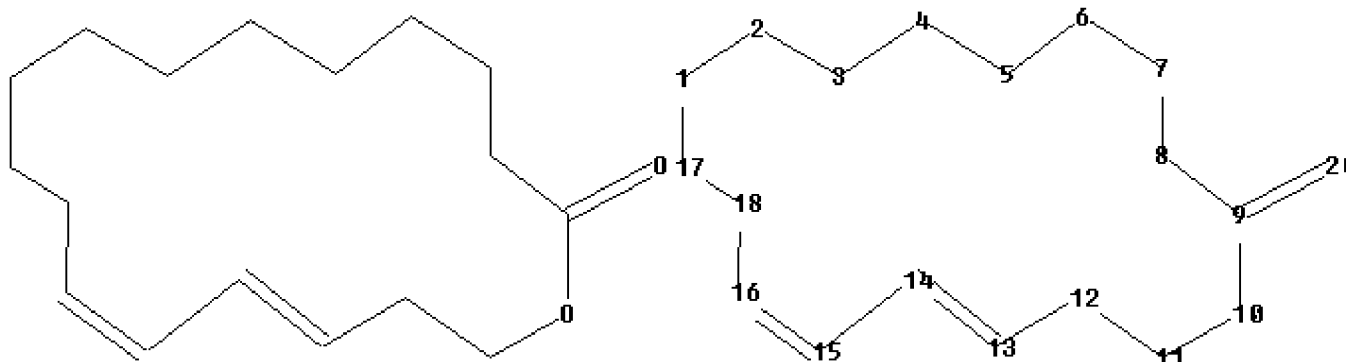
L2 SCR 2043 OR 1918

L3 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



chain nodes :

20

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

chain bonds :

9-20

ring bonds :

1-2 1-17 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-12 12-13 13-14 14-15

15-16 16-18 17-18

exact/norm bonds :

9-20

exact bonds :

1-2 1-17 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-12 12-13 13-14 14-15

15-16 16-18 17-18

isolated ring systems :

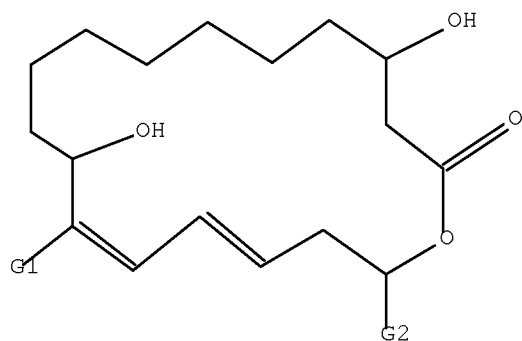
10/534210

containing 1 :

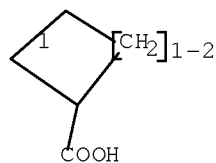
Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 20:CLASS

L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2
L6 STR



G1 Me,COOH,CN
G2 [01],[02],[03]

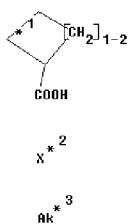
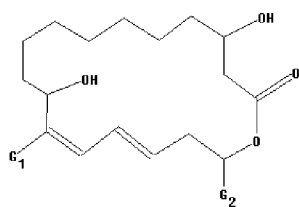


X²

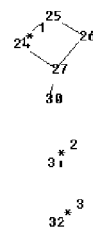
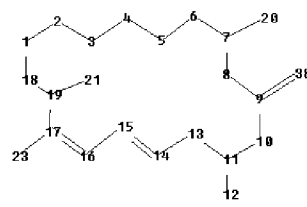
Ak³

Structure attributes must be viewed using STN Express query preparation:

Uploading L12.str



X²
Ak³



chain nodes :

12 20 21 23 30 31 32 38

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 13 14 15 16 17 18 19 24 25 26 27

chain bonds :

7-20 9-38 11-12 17-23 19-21 27-30

ring bonds :

1-2 1-18 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-13 13-14 14-15 15-16
16-17 17-19 18-19 24-25 24-27 25-26 26-27

10/534210

exact/norm bonds :

7-20 9-38 11-12 17-23 19-21

exact bonds :

1-2 1-18 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-13 13-14 14-15 15-16

16-17 17-19 18-19 24-25 24-27 25-26 26-27 27-30

isolated ring systems :

containing 1 : 24 :

G1:CH3,COOH,CN

G2:[*1],[*2],[*3]

Match level :

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11:Atom 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:CLASS 21:CLASS
23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom 30:CLASS 31:CLASS 32:CLASS
38:CLASS

L9 17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L10 86 SEA FILE=HCAPLUS ABB=ON PLU=ON L9
L11 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND 3/SC,SX
L12 5382 SEA FILE=HCAPLUS ABB=ON PLU=ON BIOSYNTHET? GENE#
L13 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND L12
L14 5465 SEA FILE=HCAPLUS ABB=ON PLU=ON POLYKETID?
L15 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND L14
L16 18 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 OR L13 OR L15
L17 19 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND PHARMAC?/SC,SX
L18 33 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 OR L17
L19 36472 SEA FILE=HCAPLUS ABB=ON PLU=ON BIOSYNTHET?
L20 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND L19
L21 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR L20
L22 478 SEA FILE=HCAPLUS ABB=ON PLU=ON SALAS J?/AU
L23 305 SEA FILE=HCAPLUS ABB=ON PLU=ON MENDEZ C?/AU
L24 51 SEA FILE=HCAPLUS ABB=ON PLU=ON OLANO C?/AU
L25 3325 SEA FILE=HCAPLUS ABB=ON PLU=ON SANCHEZ C?/AU
L26 100 SEA FILE=HCAPLUS ABB=ON PLU=ON BRANA A?/AU
L27 449 SEA FILE=HCAPLUS ABB=ON PLU=ON WILKINSON B?/AU
L28 5002 SEA FILE=HCAPLUS ABB=ON PLU=ON MARTIN C?/AU
L29 1074 SEA FILE=HCAPLUS ABB=ON PLU=ON MOSS S?/AU
L30 197 SEA FILE=HCAPLUS ABB=ON PLU=ON LEADLAY P?/AU
L31 16 SEA FILE=HCAPLUS ABB=ON PLU=ON OLIYNYK M?/AU
L42 7 SEA FILE=HCAPLUS ABB=ON PLU=ON (((L22 OR L23 OR L24 OR L25
OR L26 OR L27 OR L28 OR L29 OR L30 OR L31)) AND L10) OR (L1
AND L10)
L43 30 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 NOT L42

=> d his 134

(FILE 'MEDLINE' ENTERED AT 08:57:41 ON 04 SEP 2008)

L34 3 S L33 AND BIOSYNTHET?

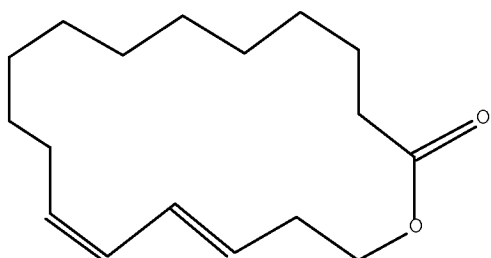
=> d que 134

L2 SCR 2043 OR 1918

10/534210

L3

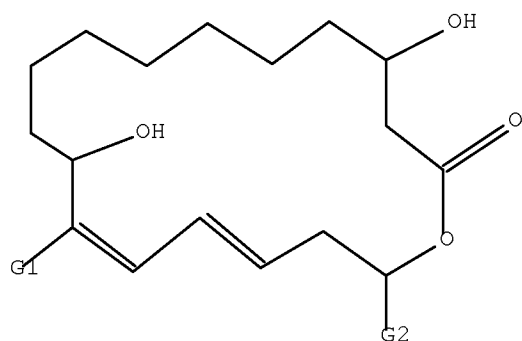
STR



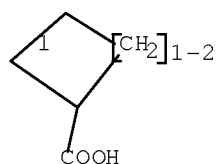
Structure attributes must be viewed using STN Express query preparation.

L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2

L6 STR



G1 Me,COOH,CN
G2 [01],[02],[03]



X²

Ak³

Structure attributes must be viewed using STN Express query preparation.

L9 17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6

L32 1 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND (MEDLINE OR BIOSIS OR DRUGU OR EMBASE)/LC

L33 31 SEA FILE=MEDLINE ABB=ON PLU=ON L32

L34 3 SEA FILE=MEDLINE ABB=ON PLU=ON L33 AND BIOSYNTHET?

=> d his 136

(FILE 'BIOSIS' ENTERED AT 08:58:27 ON 04 SEP 2008)

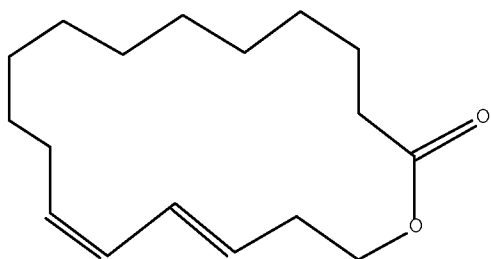
L36 6 S L33 AND BIOSYNTHET?

=> d que 136

L2 SCR 2043 OR 1918

L3 STR

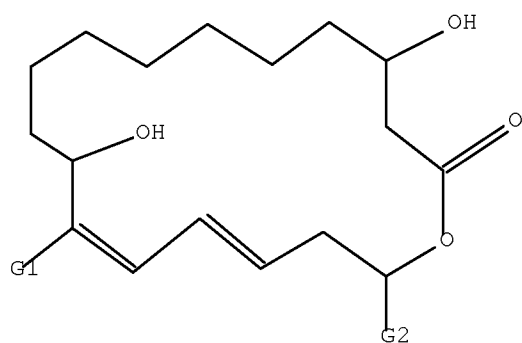
10/534210



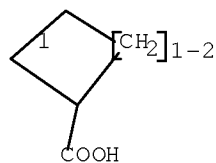
Structure attributes must be viewed using STN Express query preparation.

L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2

L6 STR



G1 Me,COOH,CN
G2 [@1],[@2],[@3]



X²

Ak³

Structure attributes must be viewed using STN Express query preparation.

L9 17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6

L32 1 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND (MEDLINE OR BIOSIS OR DRUGU OR EMBASE)/LC

L33 31 SEA FILE=MEDLINE ABB=ON PLU=ON L32

L36 6 SEA FILE=BIOSIS ABB=ON PLU=ON L33 AND BIOSYNTHET?

=> d his 138

(FILE 'DRUGU' ENTERED AT 08:58:53 ON 04 SEP 2008)

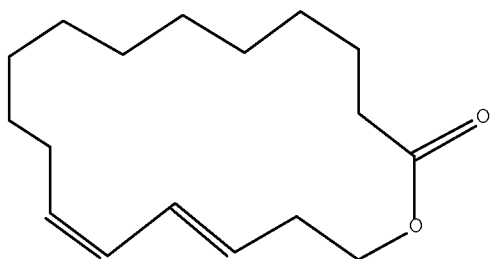
L38 8 S L33

=> d que 138

L2 SCR 2043 OR 1918

L3 STR

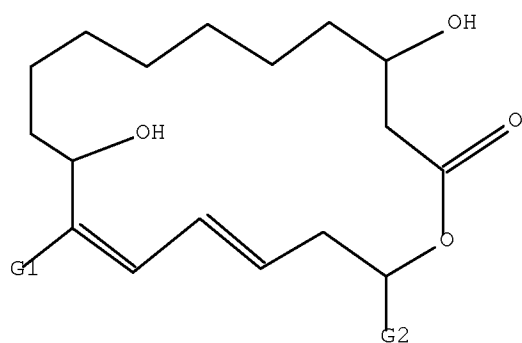
10/534210



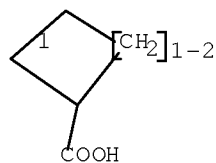
Structure attributes must be viewed using STN Express query preparation.

L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2

L6 STR



G1 Me,COOH,CN
G2 [01],[02],[03]



X 2

Ak 3

Structure attributes must be viewed using STN Express query preparation.

L9 17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6

L32 1 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND (MEDLINE OR BIOSIS OR
DRUGU OR EMBASE)/LC

L38 8 SEA FILE=DRUGU ABB=ON PLU=ON L32

=> d his 139

(FILE 'DRUGU' ENTERED AT 08:58:53 ON 04 SEP 2008)

FILE 'EMBASE' ENTERED AT 08:59:36 ON 04 SEP 2008

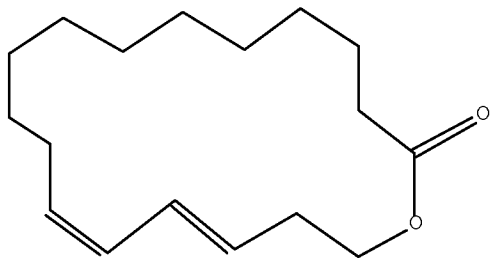
L39 3 S L33 AND BIOSYNTHET?

=> d que 139

L2 SCR 2043 OR 1918

L3 STR

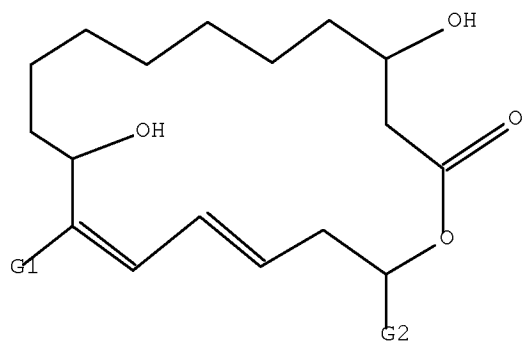
10/534210



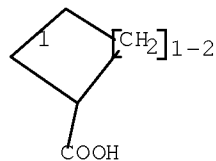
Structure attributes must be viewed using STN Express query preparation.

L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2

L6 STR



G1 Me,COOH,CN
G2 [01],[02],[03]



X²

Ak³

Structure attributes must be viewed using STN Express query preparation.

L9 17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6

L32 1 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND (MEDLINE OR BIOSIS OR DRUGU OR EMBASE)/LC

L33 31 SEA FILE=MEDLINE ABB=ON PLU=ON L32

L39 3 SEA FILE=EMBASE ABB=ON PLU=ON L33 AND BIOSYNTHET?

=> dup rem 143 134 136 138 139

FILE 'HCAPLUS' ENTERED AT 09:11:54 ON 04 SEP 2008

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE 'MEDLINE' ENTERED AT 09:11:54 ON 04 SEP 2008

FILE 'BIOSIS' ENTERED AT 09:11:54 ON 04 SEP 2008

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FILE 'DRUGU' ENTERED AT 09:11:54 ON 04 SEP 2008

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FILE 'EMBASE' ENTERED AT 09:11:54 ON 04 SEP 2008

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PROCESSING COMPLETED FOR L43

PROCESSING COMPLETED FOR L34

PROCESSING COMPLETED FOR L36

PROCESSING COMPLETED FOR L38

PROCESSING COMPLETED FOR L39

L45 40 DUP REM L43 L34 L36 L38 L39 (10 DUPLICATES REMOVED)

ANSWERS '1-30' FROM FILE HCAPLUS

ANSWERS '31-32' FROM FILE MEDLINE

ANSWER '33' FROM FILE BIOSIS

ANSWERS '34-39' FROM FILE DRUGU

ANSWER '40' FROM FILE EMBASE

=> d l45 1-30 ibib abs fhitr hitind; d l45 31-40 ibib ab hitind

L45 ANSWER 1 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2003:442770 HCAPLUS Full-text

DOCUMENT NUMBER: 139:159699

TITLE: Borrelidin induces the transcription of amino acid biosynthetic enzymes via a GCN4-dependent pathway

AUTHOR(S): Eastwood, Erin L.; Schaus, Scott E.

CORPORATE SOURCE: Metcalf Center for Science and Engineering, Department of Chemistry, Boston University, Boston, MA, 02215, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(13), 2235-2237

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Global cellular profiling of mRNA levels has been used to provide insight into the effects of the angiogenesis inhibitor borrelidin on the eukaryotic model organism *Saccharomyces cerevisiae*. The most notable result of treatment with borrelidin is the induction of amino acid biosynthetic enzymes in a time-dependent fashion. We have ascertained that induction of this pathway involves the GCN4 transcription factor. This conclusion was determined by treating a yeast strain lacking this gene and observing the absence of increased gene transcription under Gcn4p control.

IT 7184-60-3, Borrelidin

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

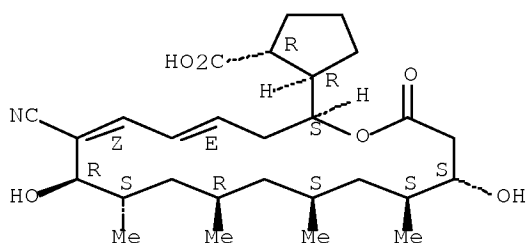
(borrelidin induces transcription of amino acid biosynthetic enzymes via a GCN4-dependent pathway)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



CC 1-8 (Pharmacology)
 ST amino acid biosynthetic enzyme borrelidin GCN4
 IT Transcription factors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (GCN4; borrelidin induces transcription of amino acid
 biosynthetic enzymes via a GCN4-dependent pathway)
 IT Transcription, genetic
 (borrelidin induces transcription of amino acid biosynthetic
 enzymes via a GCN4-dependent pathway)
 IT Amino acids, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (borrelidin induces transcription of amino acid biosynthetic
 enzymes via a GCN4-dependent pathway)
 IT 7184-60-3, Borrelidin
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (borrelidin induces transcription of amino acid biosynthetic
 enzymes via a GCN4-dependent pathway)
 REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2003:695485 HCAPLUS Full-text

DOCUMENT NUMBER: 140:70527

TITLE: Anti-angiogenesis effects of borrelidin are mediated
 through distinct pathways: Threonyl-tRNA synthetase
 and caspases are independently involved in suppression
 of proliferation and induction of apoptosis in
 endothelial cells

AUTHOR(S): Kawamura, Takanori; Liu, Diana; Towle, Murray J.;
 Kageyama, Rena; Tsukahara, Naoko; Wakabayashi,
 Toshiaki; Littlefield, Bruce A.

CORPORATE SOURCE: Eisai Research Institute, Andover, MA, 01810-2441, USA

SOURCE: Journal of Antibiotics (2003), 56(8), 709-715

CODEN: JANTAJ; ISSN: 0021-8820

PUBLISHER: Japan Antibiotics Research Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Borrelidin, an antibiotic with anti-angiogenic activity, not only suppresses
 new capillary tube formation, but also collapses formed capillary tubes in a
 rat aorta culture model. Since it selectively inhibits threonyl-tRNA
 synthetase, we examined the effect of threonine on its anti-angiogenic
 activity. We found that a high concentration of threonine (1 mM) attenuated
 the ability of borrelidin to inhibit both capillary tube formation in the rat
 aorta culture model and human umbilical vein endothelial cells (HUVEC)
 proliferation, yet did not affect the ability of borrelidin to collapse formed
 capillary tubes or to induce apoptosis in HUVEC. Borrelidin activated

caspase-3 and -8, and inhibitors of both caspase-3 and -8 suppressed borrelidin-induced apoptosis in HUVEC. Taken together, these data suggest that the anti-angiogenic effects of borrelidin are mediated through at least two mechanisms, i.e. one threonine-dependent and the other threonine-independent, and borrelidin induces apoptosis in endothelial cells via the caspase-8/-3 pathway.

IT 7184-60-3, Borrelidin

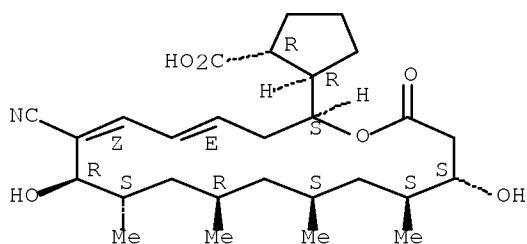
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of antiangiogenic effects of borrelidin)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



CC 1-6 (Pharmacology)

IT 7184-60-3, Borrelidin

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of antiangiogenic effects of borrelidin)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 1997:578984 HCAPLUS Full-text

DOCUMENT NUMBER: 127:242909

ORIGINAL REFERENCE NO.: 127:47239a, 47242a

TITLE: Borrelidin is an angiogenesis inhibitor; disruption of angiogenic capillary vessels in a rat aorta matrix culture model

AUTHOR(S): Wakabayashi, Toshiaki; Kageyama, Rena; Naruse, Nobuaki; Tsukahara, Naoko; Funahashi, Yasuhiro; Kitoh, Kyosuke; Watanabe, Yoshio

CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai, Co., Ltd., Tsukuba, 300-26, Japan

SOURCE: Journal of Antibiotics (1997), 50(8), 671-676
CODEN: JANTAJ; ISSN: 0021-8820

PUBLISHER: Japan Antibiotics Research Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Borrelidin, an antibiotic from *Streptomyces rochei*, was found to be an angiogenesis inhibitor in a rat aorta matrix culture model which forms capillary vessels in vitro. Borrelidin strongly inhibited capillary tube formation with a 50%-inhibitory concentration value of 0.8 nM, and decreased

10/534210

the number of capillary tubes within 24 h when added after maturation of tube formation. Borrelidin remarkably disrupted capillary tubes in a dose-dependent manner, by inducing apoptosis of the tube-forming cells.

IT 7184-60-3, Borrelidin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

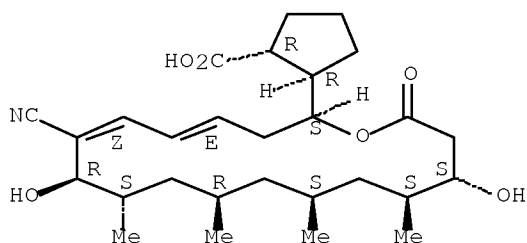
(angiogenesis inhibition by borrelidin)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



CC 1-6 (Pharmacology)

IT 7184-60-3, Borrelidin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(angiogenesis inhibition by borrelidin)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1971:20712 HCAPLUS Full-text

DOCUMENT NUMBER: 74:20712

ORIGINAL REFERENCE NO.: 74:3331a,3334a

TITLE: Effect of borrelidin on the threonyl-tRNA-synthetase activity and the regulation of threonine-biosynthetic enzymes in *Saccharomyces cerevisiae*

AUTHOR(S): Nass, Gisela; Hasenbank, R.

CORPORATE SOURCE: Max-Planck-Inst. Mol. Genet., Berlin, Fed. Rep. Ger.

SOURCE: Molecular and General Genetics (1970), 108(1), 28-32
CODEN: MGGEAE; ISSN: 0026-8925

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Threonyl-tRNA (transfer RNA) synthetase and aspartokinase levels were depressed 20- and 2-fold, resp., when yeast cells were grown in the presence of 0.5 g/ml borrelidin. When threonine (0.37 mg/ml) or homo-serine (1.4 mg/ml) was included in the medium, borrelidin had no effect on aspartokinase level. Threonyl-tRNA synthetase may be involved in repression of formation of the threonine bio-synthetic enzyme.

IT 7184-60-3

RL: BIOL (Biological study)

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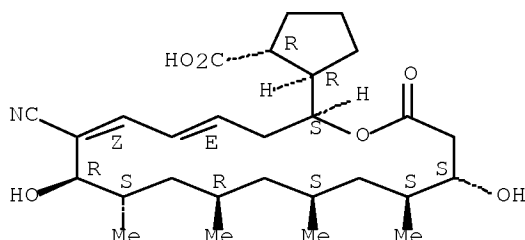
(threonine-forming enzymes inhibition by, in *Saccharomyces cerevisiae*)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



CC 8 (Microbial Biochemistry)

IT 7184-60-3

RL: BIOL (Biological study)

(threonine-forming enzymes inhibition by, in *Saccharomyces cerevisiae*)

L45 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 1969:55138 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 70:55138

ORIGINAL REFERENCE NO.: 70:10353a,10356a

TITLE: Effect of the antibiotic, borrelidin, on the regulation of threonine biosynthetic enzymes in *Escherichia coli*

AUTHOR(S): Nass, Gisela; Poralla, K.; Zaehner, Hans

CORPORATE SOURCE: Max-Planck-Inst. Mol. Genet., Berlin, Fed. Rep. Ger.

SOURCE: Biochemical and Biophysical Research Communications (1969), 34(1), 84-91

CODEN: BBRCA9; ISSN: 0006-291X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Borrelidin (0.7 or 7.0 $\mu\text{g./ml.}$) almost abolished threonyl-tRNA synthetase activity in cell-free exts. of *E. coli* K12 or *E. coli* B; it did not affect methionyl-tRNA, arginyl-tRNA, phenylalanyl-tRNA, isoleucyl-tRNA, leucyl-tRNA, tyrosyl-tRNA, lysyl-tRNA, or valyl-tRNA synthetases. In the presence of borrelidin (7 $\mu\text{g./ml.}$) the growth rate of the bacteria was halved, while the sp. activities of aspartokinase and homoserine dehydrogenase increased 4-6-fold; threonine deaminase activity remained unchanged, demonstrating the specificity of the derepression process. When *E. coli* were grown in the presence of threonine (100 $\mu\text{g./ml.}$) and borrelidin (21 $\mu\text{g./ml.}$), growth limitation was almost abolished but a 3-fold derepression of threonine-specific aspartokinase was still observed. Borrelidin inhibits threonyl-tRNA synthetase in vivo, thus limiting the production of threonine-charged RNA and leading to growth inhibition. Also, inhibition of threonyl-tRNA synthetase by borrelidin derepressed threonine biosynthetic enzymes, since the formation of repressor from threonine by the threonyl-tRNA synthetase was also impaired.

IT 7184-60-3

RL: BIOL (Biological study)

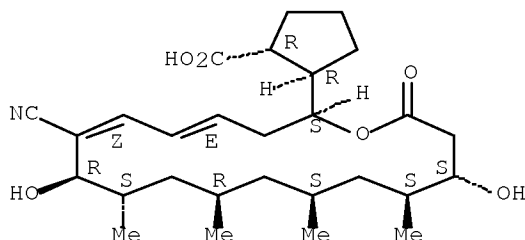
(threonine formation inhibition by)

RN 7184-60-3 HCAPLUS

10/534210

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 8 (Microbial Biochemistry)
IT 7184-60-3
RL: BIOL (Biological study)
(threonine formation inhibition by)

L45 ANSWER 6 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:315049 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 146:513453

TITLE: Mutasynthesis - uniting chemistry and genetics for drug discovery

AUTHOR(S): Weissman, Kira J.

CORPORATE SOURCE: Department of Biochemistry, University of Cambridge, Cambridge, CB2 1GA, UK

SOURCE: Trends in Biotechnology (2007), 25(4), 139-142
CODEN: TRBIDM; ISSN: 0167-7799

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Mutasynthesis couples the power of chemical synthesis with mol. biol. to generate derivs. of medicinally valuable, natural products. Recently, this technique has been exploited by Cambridge-based biotech company Biotica Technol. Ltd, and their collaborators, to generate promising new variants of the polyketide anti-cancer compds. rapamycin and borrelidin.

IT 7184-60-3P, Borrelidin

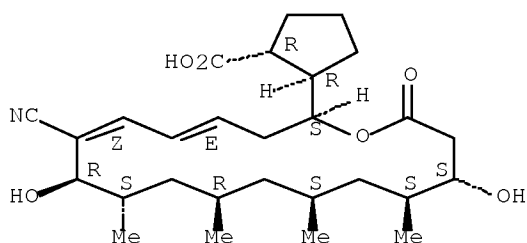
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(mutasynthesis - uniting chemical and genetics for drug discovery)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 1-0 (Pharmacology)
 IT 7184-60-3P, Borrelidin 53123-88-9P, Rapamycin
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (mutasynthesis - uniting chemical and genetics for drug discovery)
 REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 7 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:1256641 HCAPLUS Full-text
 DOCUMENT NUMBER: 146:50262
 TITLE: Antibiotic kit and compositions
 INVENTOR(S): Friedman, Doron; Besonov, Alex; Tamarkin, Dov; Eini,
 Meir
 PATENT ASSIGNEE(S): Foamix Ltd., Israel
 SOURCE: U.S. Pat. Appl. Publ., 31pp., Cont.-in-part of U.S.
 Ser. No. 532,618.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 28
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060269485	A1	20061130	US 2006-448490	20060607
WO 2004037225	A2	20040506	WO 2003-IB5527	20031024
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US 20050069566	A1	20050331	US 2004-911367	20040804
US 20060140984	A1	20060629	US 2005-532618	20051222
AU 2006339311	A2	20070907	AU 2006-339311	20060607
AU 2006339311	A1	20070907		
CA 2611577	A1	20070907	CA 2006-2611577	20060607
WO 2007099396	A2	20070907	WO 2006-IB3975	20060607
WO 2007099396	A3	20080313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				

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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
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SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

EP 1919449 A2 20080514 EP 2006-847249 20060607

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
BA, HR, MK, RS

US 20070292355 A1 20071220 US 2007-732547 20070404

WO 2008075207 A2 20080626 WO 2007-IB4459 20070404

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,
GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT,
RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM

IN 2007KN04925 A 20080704 IN 2007-KN4925 20071218

PRIORITY APPLN. INFO.:

US 2002-429546P P 20021129
US 2003-492385P P 20030804
WO 2003-IB5527 W 20031024
US 2004-911367 A2 20040804
US 2005-688244P P 20050607
US 2005-532618 A2 20051222
IL 2002-152486 A 20021025
US 2003-497648P P 20030825
US 2003-530015P P 20031216
US 2004-835505 A2 20040428
US 2004-922358 A2 20040820
US 2005-41921 A2 20050124
US 2006-789186P P 20060404
US 2006-448490 A2 20060607
WO 2006-IB3975 W 20060607
US 2006-861620P P 20061129
US 2007-880434P P 20070112

AB The present invention relates to a therapeutic kit to provide an effective dosage of an antibiotic including an aerosol packaging assembly. The assembly includes a container accommodating a pressurized product; and an outlet capable of releasing the pressurized product as a foam, wherein the pressurized product comprises a foamable composition of an antibiotic; at least one organic carrier selected from the group consisting of a hydrophobic organic carrier, an organic polar solvent, an emollient and mixts. at 2-50%, a surfactant, 0.01-5% by weight of at least one polymeric additive selected from the group consisting of a bioadhesive agent, a gelling agent, a film forming agent and a phase change agent, water; and liquefied or compressed gas propellant at 3-25% by weight of the total composition

IT 7184-60-3, Treponemycin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

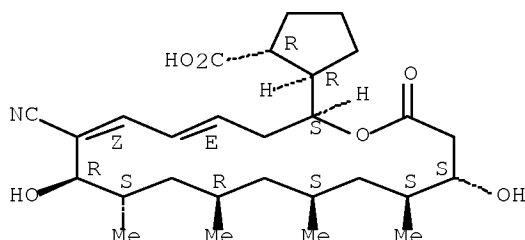
(antibiotic kit and compns.)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



INCL 424045000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 62

IT 6833-84-7, Nonactin 6834-98-6, Pentamycin 6980-18-3, Kasugamycin 6990-06-3, Fusidic acid 6990-06-3D, Fusidic acid, derivs. 6998-60-3, Rifamycin 7177-48-2, Ampicillin trihydrate 7184-60-3, Treponemycin 7229-50-7, Streptolydigin 7440-22-4, Silver, biological studies 7440-44-0, Carbon, biological studies 7542-37-2, Catenulin 7553-56-2, Iodine, biological studies 7631-86-9, Silicon oxide, biological studies 7681-93-8, Natamycin 7722-84-1, Hydrogen peroxide, biological studies 7761-88-8, Silver nitrate, biological studies 7778-54-3, Calcium hypochlorite 7782-44-7, Oxygen, biological studies 7783-96-2, Silver iodide 7783-97-3, Silver iodate 8025-81-8, Foromacidin 8044-71-1, Cetrime 8064-90-2, Sulfamethoxazole-trimethoprim mixture 8065-41-6, Aureofungin 9000-07-1, Carrageenan gum 9000-30-0, Guar gum 9000-40-2, Locust bean gum 9000-65-1, Tragacanth gum 9001-63-2, Lysozyme 9004-30-2, Hydroxyethylcarboxymethylcellulose 9004-32-4, Carboxymethylcellulose 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methylcellulose 9004-67-5, Methylcellulose 9008-54-2, Circulin 9008-55-3, Coliformin 9014-02-2, Neocarcinostatin 9032-42-2, Methylhydroxyethylcellulose 10023-07-1, Frenolicin 10118-90-8, Minocycline 10233-03-1, Magnesium hypochlorite 11003-33-1, Bleomycin B 11003-38-6, Capreomycin 11005-09-7, Phytoactin 11005-96-2, Danomycin 11005-98-4, Destomycin B 11006-22-7, Flavofungin 11006-33-0, Phleomycin 11006-64-7, Iyomycin 11006-70-5, Olivomycin 11006-76-1, Mikamycin 11006-83-0, Thermorubin 11011-72-6, Bluensomycin 11014-70-3, Levorin 11015-37-5, Moenomycin 11016-07-2, Perimycin 11016-19-6, Phytostreptin 11016-29-8, Polcillin 11016-71-0, Rubiflavin 11016-72-1, Rubomycin 11017-43-9, Siomycin 11021-88-8, Venturicidin 11030-68-5, Desdamethine 11031-38-2, Rubradirin 11031-48-4, Sarkomycin 11032-08-9, Theriothiocin 11033-34-4, Steffimycin 11043-99-5, Mitomalcin 11048-13-8, Nebramycin 11048-97-8, Hedamycin 11051-71-1, Avilamycin 11052-01-0, Ericamycin 11054-63-0, Tsushimycin 11056-20-5, Zorbamycin 11075-36-8, Tuberactinomycin 11078-21-0, Filipin 11078-23-2, Copiamycin 11079-53-1, Hyperforin 11089-65-9, Tunicamycin 11096-49-4, Partricin 11111-12-9, Cephalosporin 11111-23-2, Lividomycin 11113-62-5, Enniatin 11113-64-7, Imanine

11113-76-1, Quinomycin 11113-80-7, Polyoxin 11113-83-0, Roridin
 11115-82-5, Enduracidin 11118-72-2, Antimycin 11121-32-7, Mepartricin
 11130-70-4, Saramycetin 11138-66-2, Xanthan gum 11141-18-7, Diumycin
 12001-79-5, Vitamin K 12001-79-5D, Vitamin K, derivs. 12609-84-6,
 Thiopeptin 12619-70-4, Cyclodextrin 12633-72-6, Amphotericin
 12633-72-6D, Amphotericin, Me derivs. 12634-34-3, Macromomycin
 12650-69-0, Mupirocin 12676-71-0, Niphimycin 12688-25-4, Jolipeptin
 12689-28-0, Proticin 12698-52-1, Dermadin 12704-90-4, Aurodox
 12772-35-9, Butirosin 13058-67-8, Lucensomycin 13182-89-3,
 Metronidazole benzoate 13292-46-1, Rifampicin 13410-30-5,
 6-Azathymidine 13463-67-7, Titanium dioxide, biological studies
 13614-98-7, Minocycline hydrochloride 13838-08-9, Azidamfenicol
 13929-35-6, Nancimycin 13929-35-6D, Nancimycin, derivs. 14698-29-4,
 Oxolinic acid 14807-96-6, Talc, biological studies 14918-35-5,
 Destomycin A 15318-45-3, Thiamphenicol 15387-18-5, Fezatione
 15686-71-2, Cephalixin 15768-18-0, Silver lactate 16055-12-2
 16755-07-0, Showdomycin 16773-42-5, Ornidazole 16846-24-5, Josamycin
 16887-00-6, Perchloride, biological studies 17090-79-8, Monensin
 17243-38-8, Azidocillin 17397-89-6, Cerulenin 17650-86-1, Amicetin
 18268-45-6, Silver laurate 18323-44-9, Clindamycin 18472-51-0,
 Chlorhexidine gluconate 18883-66-4, Streptozocin 19246-24-3, Telomycin
 19387-91-8, Tinidazole 19504-77-9, Variotin 19562-30-2, Piromidic acid
 19721-56-3, Picromycin 19879-06-2, Granaticin 19889-01-1, Arctiopicrin
 20283-48-1, Chalcomycin 20283-69-6, Niddamycin 20350-15-6, Brefeldin
 20667-12-3, Silver oxide 20830-81-3, Daunorubicin 21593-23-7,
 Cefapirin 21612-26-0, β -Alanyl-L-tyrosine 22199-08-2,
 Sulfadiazine silver 22332-07-6, Hybrimycin A1 22332-08-7, Hybrimycin
 B1 22400-60-8, Hybrimycin A2 22573-93-9, Alexidine 22733-60-4,
 Siccanin 22832-87-7, Miconazole nitrate 22862-76-6, Anisomycin
 22916-47-8, Miconazole 22976-87-0, Polyoxine 23110-15-8, Fumagillin
 23155-02-4, Fosfomycin 23214-92-8, Doxorubicin 23239-41-0
 23363-64-6, Chlorflavonin 23477-98-7, Sedecamycin 23510-81-8, Humulone
 23593-75-1, Clotrimazole 23668-11-3, Pactamycin 24168-96-5,
 Isoconazole nitrate 24169-02-6, Econazole nitrate 24394-09-0, Cnicin
 24751-69-7, Nucleocidin 25265-75-2, Butylene glycol 25316-40-9,
 Doxorubicin hydrochloride 25322-68-3, Polyethylene glycol 25389-94-0,
 Kanamycin sulfate 25546-65-0, Ribostamycin 25953-19-9, Cefazolin
 25999-31-9, Lasalocid 26774-90-3, Epicillin 26786-84-5, Lomofungin
 26787-78-0, Amoxicillin 26973-24-0, Ceftezole 27025-49-6, Carfecillin
 27208-79-3, Trehalosamine 27220-47-9, Econazole 27267-69-2,
 Collinomycin 27425-78-1, Hybrimycin B2 27523-40-6, Isoconazole
 27726-31-4 28002-70-2, Framycetin sulfate 28069-65-0, Cuprimyxin
 28399-50-0, Rabelomycin 28657-80-9, Cinoxacin 28978-07-6, Anticapsin
 29144-42-1, Cetocycline 29342-05-0, Ciclopirox 29382-82-9,
 Flavensomycin 30042-37-6, Lankamycin 30868-30-5, Pyrazomycin
 31282-04-9, Hygromycin B 31692-85-0, Glycofurol 32385-11-8, Sisomicin
 32886-97-8, Pivmecillinam 32887-01-7, Mecillinam 32887-03-9,
 Pivmecillinam hydrochloride 32986-56-4, Tobramycin 32988-50-4
 33817-20-8, Pivampicillin 34051-04-2, 3'-Deoxyneamine 34291-03-7,
 Butirosin B 34444-01-4, Cefamandole 34493-98-6, Dibekacin
 34642-77-8, Amoxicillin sodium 34787-01-4, Ticarcillin 35025-95-7,
 3',4'-Dideoxyneamine 35457-80-8, Midecamycin 35531-88-5, Carindacillin
 35554-44-0, Enilconazole 35607-66-0, Cefoxitin 35663-85-5,
 Cyclamidomycin 35818-31-6, Cladosporin 35818-32-7, Monomethyl
 cladosporin 35818-33-8, Monoacetyl cladosporin 35834-26-5, Rosaramicin
 35846-53-8, Maytansine 35865-33-9, Dianemycin 35891-70-4, Myriocin
 36653-82-4, Cetyl alcohol 37065-29-5, Miloxacin 37091-66-0, Azlocillin
 37217-63-3 37217-65-5, Candimycin 37231-28-0, Melittin
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antibiotic kit and compns.)

L45 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:1176162 HCAPLUS Full-text
 DOCUMENT NUMBER: 145:470057
 TITLE: Process for the preparation of L-threonine using
 bacteria of the Enterobacteriaceae family
 INVENTOR(S): Kruse, Daniela; Hermann, Thomas; Thierbach, Georg;
 Rieping, Mechthild
 PATENT ASSIGNEE(S): Degussa AG, Germany
 SOURCE: U.S. Pat. Appl. Publ., 25pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060252133	A1	20061109	US 2006-566606	20060511
WO 2005014842	A1	20050217	WO 2004-EP8390	20040727
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
 DE 2003-10335253 A 20030801
 US 2003-491981P P 20030804
 DE 2004-102004230552A 20040511
 DE 2004-102004288593A 20040615
 WO 2004-EP8390 W 20040727
 DE 2004-102004023055A 20040511
 DE 2004-102004028859A 20040615

AB The invention relates to an improved process for the fermentative preparation
 of L-threonine using bacteria of the Enterobacteriaceae family which produce
 L-threonine.

IT 7184-60-3, Borrelidin

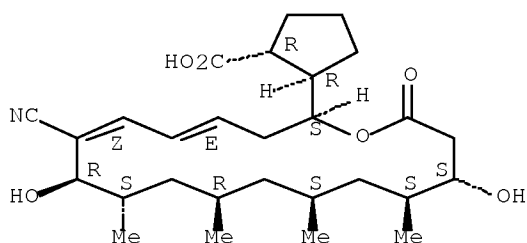
RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (resistance to; process for preparation of L-threonine using bacteria of
 Enterobacteriaceae family)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-
 8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-
 yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



INCL 435106000; 435252330

CC 16-2 (Fermentation and Bioindustrial Chemistry)

Section cross-reference(s): 3

IT 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, L-Lysine, biological studies 98-83-9, α -Methylstyrene, biological studies 921-52-8, Diaminosuccinic acid 7184-60-3, Borrelidin 13292-46-1, Rifampicin

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance to; process for preparation of L-threonine using bacteria of Enterobacteriaceae family)

L45 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:937808 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 145:471283

TITLE: o-DPPB-directed copper-mediated allylic substitution:
Part 2; Iterative deoxypropionate synthesis based on a
copper-mediated directed allylic substitution: formal
total synthesis of borrelidin (C3-C11 fragment)

AUTHOR(S): Herber, Christian; Breit, Bernhard

CORPORATE SOURCE: Inst. Org. Chem. Biochem., Albert-Ludwigs-Univ.
Freiburg, Freiburg, 79104, Germany

SOURCE: Chemistry--A European Journal (2006), 12(25),
6684-6691

CODEN: CEUJED; ISSN: 0947-6539

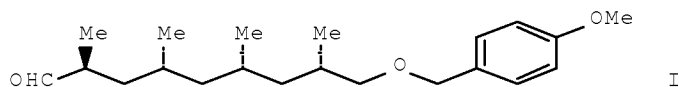
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 145:471283

GI



AB A new iterative strategy for the flexible preparation of any oligodeoxypropionate stereoisomer is presented which relies on an o-DPPB-directed copper-mediated allylic substitution employing enantiomerically pure Grignard reagents. This key C-C bond-forming step features reversed polarity compared with established enolate alkylation methodol. It thus avoids existing problems of enolate alkylation strategies such as enolate reactivity as well as costs and problems associated with the chiral auxiliary. Practicability of this new method is demonstrated through application in

natural product syntheses. Thus, an efficient synthesis of the northern part of the angiogenesis inhibitor borrelidin, the deoxypropionate building block I, could be devised, representing a formal total synthesis.

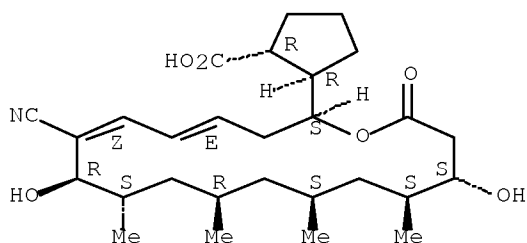
IT 7184-60-3F

RL: PNU (Preparation, unclassified); PREP (Preparation)
(iterative deoxypropionate synthesis based on a copper-mediated directed allylic substitution and the formal total synthesis of borrelidin)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 26-6 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 23

ST deoxypropionate asym synthesis copper mediated allylic substitution
Grignard Umpolung; formal synthesis polyketide borrelidin

IT Polyketides

RL: PNU (Preparation, unclassified); PREP (Preparation)
(iterative deoxypropionate synthesis based on a copper-mediated directed allylic substitution and the formal total synthesis of borrelidin)

IT 7184-60-3F

RL: PNU (Preparation, unclassified); PREP (Preparation)
(iterative deoxypropionate synthesis based on a copper-mediated directed allylic substitution and the formal total synthesis of borrelidin)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:141256 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:238754

TITLE: Fermentative preparation of L-threonine using recombinant Escherichia coli

INVENTOR(S): Kruse, Daniela; Hermann, Thomas; Thierbach, Georg; Rieping, Mechthild

PATENT ASSIGNEE(S): Degussa A.-G., Germany

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

AB	The invention provides an improved process for the fermentative preparation of L-threonine using L-threonine-producing bacteria from the family Enterobacteriaceae. In particular, the invention provides a recombinant strain of Escherichia coli in which a threonine-insensitive aspartate kinase gene (thrA) is overexpressed and the rpoS gene is attenuated by inserting a stop codon into its coding sequence. Addnl., the invention provides a fed-batch or repeat-batch fermentation process for the production of L-threonine.
IT	7184-60-3, Borrelidin
RL	BSU (Biological study, unclassified); BIOL (Biological study) (fermentative preparation of L-threonine using recombinant Escherichia coli)
RN	7184-60-3 HCAPLUS
CN	Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

40

10/534210

CC 16-2 (Fermentation and Bioindustrial Chemistry)
 Section cross-reference(s): 3
 IT 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid,
 biological studies 56-87-1, L-Lysine, biological studies 63-68-3,
 L-Methionine, biological studies 433-48-7, Fluoropyruvic acid
 921-52-8, Diaminosuccinic acid 922-54-3 5424-29-3,
 α -Methylserine 7184-60-3, Borrelidin 13292-46-1,
 Rifampin
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (fermentative preparation of L-threonine using recombinant Escherichia
 coli)

L45 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2005:141255 HCAPLUS Full-text
 DOCUMENT NUMBER: 142:238753
 TITLE: Fermentative preparation of L-threonine using
 recombinant Escherichia coli
 INVENTOR(S): Kruse, Daniela; Hermann, Thomas; Thierbach, Georg;
 Rieping, Mechthild
 PATENT ASSIGNEE(S): Degussa A.-G., Germany
 SOURCE: PCT Int. Appl., 67 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014842	A1	20050217	WO 2004-EP8390	20040727
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004028859	A1	20050224	DE 2004-102004028859	20040615
EP 1649033	A1	20060426	EP 2004-763525	20040727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1829801	A	20060906	CN 2004-80021728	20040727
BR 2004013139	A	20061003	BR 2004-13139	20040727
US 20060252133	A1	20061109	US 2006-566606	20060511
PRIORITY APPLN. INFO.:			DE 2003-10335253	A 20030801
			US 2003-491981P	P 20030804
			DE 2004-102004023055A	20040511
			DE 2004-102004028859A	20040615
			DE 2004-102004230552A	20040511
			DE 2004-102004288593A	20040615
			WO 2004-EP8390	W 20040727

AB The invention provides an improved process for the fermentative preparation of
 L-threonine using L-threonine-producing bacteria from the family
 Enterobacteriaceae. In particular, the invention provides a recombinant
 strain of Escherichia coli in which a threonine-insensitive aspartate kinase
 gene (thrA) is overexpressed and the rpoS gene is attenuated by inserting a

10/534210

stop codon into it coding sequence. Addnl., the invention provides a fed-batch or repeat-batch fermentation process for the production of L-threonine.

IT 7184-60-3, Borrelidin

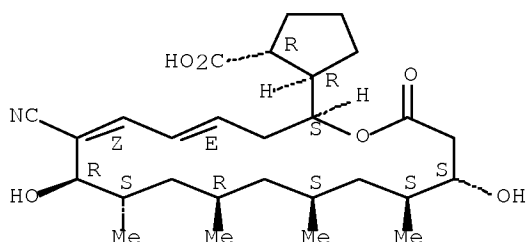
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fermentative preparation of L-threonine using recombinant Escherichia coli)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IC ICM C12P013-08

ICS C12R001-19

CC 16-2 (Fermentation and Bioindustrial Chemistry)

Section cross-reference(s): 3

IT 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, L-Lysine, biological studies 63-68-3, L-Methionine, biological studies 433-48-7, Fluoropyruvic acid 921-52-8, Diaminosuccinic acid 922-54-3 5424-29-3, α -Methylserin 7184-60-3, Borrelidin 13292-46-1, Rifampin

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fermentative preparation of L-threonine using recombinant Escherichia coli)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:141254 HCAPLUS Full-text

DOCUMENT NUMBER: 142:238752

TITLE: Fermentative preparation of L-threonine using recombinant Escherichia coli using a cell-recycle fermentor

INVENTOR(S): Kruse, Daniela; Hermann, Thomas; Rieping, Mechthild; Thierbach, Georg

PATENT ASSIGNEE(S): Degussa A.-G., Germany

SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----

DE 102004029340	A1	20050224	DE 2004-102004029340	20040617
EP 1649032	A1	20060426	EP 2004-763524	20040727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

DE	2003-10335254	A	20030801
US	2003-491982P	P	20030804
DE	2004-102004029340A		20040617
WO	2004-EP8389	W	20040727

IT 7184-60-3, Borrelidin

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 3

43

10/534210

921-52-8, Diaminosuccinic acid 922-54-3 5424-29-3, α -Methylserin
7184-60-3, Borrelidin 13292-46-1, Rifampin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fermentative preparation of L-threonine using recombinant Escherichia coli
using cell-recycle fermentor)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:801181 HCAPLUS Full-text

DOCUMENT NUMBER: 141:271534

TITLE: Remedies and/or preventives for Plasmodium infection
containing borrelidin

INVENTOR(S): Omura, Satoru; Otoguro, Kazuhiko; Yamada, Haruki; Ui,
Hideaki

PATENT ASSIGNEE(S): Kitasato Institute, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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JP 2004269440	A	20040930	JP 2003-63769	20030310
PRIORITY APPLN. INFO.:			JP 2003-63769	20030310

AB The invention provides remedies and/or preventives for Plasmodium infection
caused by Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, and
Plasmodium ovale, etc., wherein the agent is characterized by containing
borrelidin as an active component. The antimalarial effect of borrelidin
against drug resistant Plasmodium yoelii NS in mice was examined

IT 7184-60-3, Borrelidin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

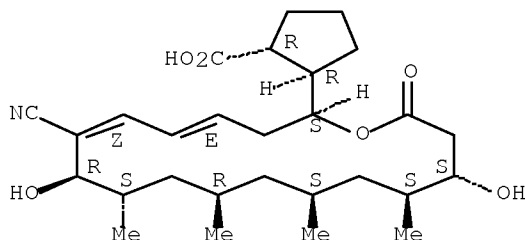
(remedies and/or preventives for Plasmodium infection containing
borrelidin)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-
8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-
yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IC ICM A61K031-365

ICS A61P033-06; C07D313-00; C12P017-08

CC 1-5 (Pharmacology)
 Section cross-reference(s): 63
 IT 7184-60-3, Borrelidin
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (remedies and/or preventives for Plasmodium infection containing
 borrelidin)

L45 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:256479 HCAPLUS Full-text

DOCUMENT NUMBER: 136:278229

TITLE: Escherichia mutants expressing chromosome-inserted
 thrABC operon from non-native promoter and their use
 in threonine production

INVENTOR(S): Liaw, Hungming James; Bradshaw, Jill S.; Yang, Yueqin;
 Mao, Weiying

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

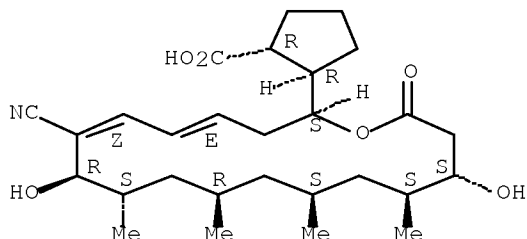
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026993	A1	20020404	WO 2001-US30558	20010928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,				
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,				
UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,				
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20020106800	A1	20020808	US 2001-962303	20010926
US 7220571	B2	20070522		
CA 2423870	A1	20020404	CA 2001-2423870	20010928
AU 2001096415	A	20020408	AU 2001-96415	20010928
EP 1322765	A1	20030702	EP 2001-977282	20010928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014101	A	20061114	BR 2001-14101	20010928
AU 2001296415	B2	20070104	AU 2001-296415	20010928
MX 2003PA02683	A	20030910	MX 2003-PA2683	20030327
US 20070254337	A1	20071101	US 2007-786818	20070413
US 20080166788	A1	20080710	US 2008-51064	20080319
PRIORITY APPLN. INFO.:			US 2000-235884P	P 20000928
			US 2001-962303	A3 20010926
			WO 2001-US30558	W 20010928
			US 2007-786818	A3 20070413

AB Escherichia coli, containing a thrABC operon under control of a non-native promoter (such as tac) inserted into the chromosome, and the use of these E. coli strains for the fermentative production of threonine are disclosed. Addnl., the thrA gene may encode a feedback-resistant aspartate kinase-homoserine dehydrogenase, or the E. coli may be mutated to resistance to threonine raffinose, borrelidin, or cyclopentanecarboxylic acid. One such recombinant E. coli produced 96.2 g L-threonine/L in fermentor culture (relative to the parent strain which produced 5.1 g/L).

IT 7184-60-3, Borrelidin
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (E. coli resistant to; escherichia mutants expressing
 chromosome-inserted thrABC operon from non-native promoter and their
 use in threonine production)
 RN 7184-60-3 HCAPLUS
 CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-
 8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-
 yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



IC ICM C12N015-52
 ICS C12P013-08
 CC 16-2 (Fermentation and Bioindustrial Chemistry)
 Section cross-reference(s): 3, 10
 IT 3400-45-1, Cyclopentanecarboxylic acid 7184-60-3, Borrelidin
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (E. coli resistant to; escherichia mutants expressing
 chromosome-inserted thrABC operon from non-native promoter and their
 use in threonine production)
 REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 15 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2002:172047 HCAPLUS Full-text
 DOCUMENT NUMBER: 136:215515
 TITLE: Fermentation of L-threonine with transgenic
 microorganisms carrying the thrABC operon
 INVENTOR(S): Hermann, Thomas; Rieping, Mechthild
 PATENT ASSIGNEE(S): Degussa AG, Germany
 SOURCE: PCT Int. Appl., 39 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018543	A2	20020307	WO 2001-EP8603	20010725
WO 2002018543	A3	20030103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

10/534210

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10103778	A1	20020314	DE 2001-10103778	20010127
AU 2002020542	A	20020313	AU 2002-20542	20010725
EP 1313838	A2	20030528	EP 2001-984568	20010725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1630711	A	20050622	CN 2001-814966	20010725
MX 2003PA00585	A	20030606	MX 2003-PA585	20030120
ZA 2003001636	A	20040203	ZA 2003-1636	20030227

PRIORITY APPLN. INFO.:

DE 2000-10042745	A	20000831
DE 2001-10103778	A	20010127
WO 2001-EP8603	W	20010725

AB The invention relates to a process for the fermentative preparation of L-threonine in which an L-threonine-producing microorganism of the Enterobacteriaceae family is cultured by the feed process, and a portion of the fermentation broth is then separated off in order to be utilized for inoculation of further media. The use of the thrABC to increase the levels of enzymes of threonine biosynthesis is demonstrated. The parB gene is used to stabilize the plasmid carrying the thrABC operon. Strains are also resistant to the adverse effects of high concns. of threonine. The space-time yield of threonine from transgenic Escherichia coli was up to 1.94 g/L+h compared to 1.76 g/L+h for the parental strain.

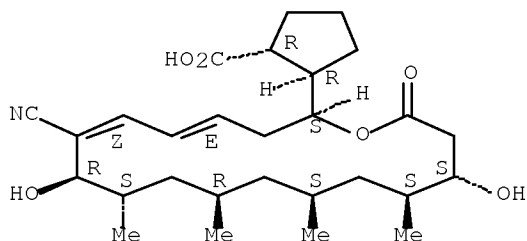
IT 7184-60-3, Borrelidin

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance to, in threonine-fermenting microorganisms; fermentation of L-threonine with transgenic microorganisms carrying thrABC operon)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM C12N001-21

ICS C12P013-08; C12N001-21; C12R001-19

CC 16-2 (Fermentation and Bioindustrial Chemistry)

Section cross-reference(s): 3, 10

IT 56-86-0, L-Glutamic acid, biological studies 921-52-8, Diaminosuccinic acid 5424-29-3, α -Methylserine 7184-60-3, Borrelidin

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance to, in threonine-fermenting microorganisms; fermentation of L-threonine with transgenic microorganisms carrying thrABC operon)

L45 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:101120 HCAPLUS Full-text

DOCUMENT NUMBER: 134:147437

TITLE: Preparation of borrelidin derivatives for
pharmaceutical use as angiogenesis inhibiting agentsINVENTOR(S): Makk, Nandor; Ambrus, Gabor; Tegdes, Aniko; Jeney,
Andras; Timar, Ferenc

PATENT ASSIGNEE(S): Gyogyszerkutato Intezet Kft., Hung.

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

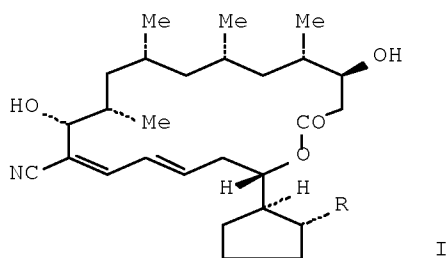
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009113	A2	20010208	WO 2000-HU88	20000802
WO 2001009113	A3	20010614		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
HU 9902628	A2	20010528	HU 1999-2628	19990802
HU 9902628	A3	20010730		
CA 2378176	A1	20010208	CA 2000-2378176	20000802
BR 2000012968	A	20020514	BR 2000-12968	20000802
EP 1206462	A2	20020522	EP 2000-949831	20000802
EP 1206462	B1	20030528		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
HU 2002002197	A2	20021028	HU 2002-2197	20000802
HU 2002002197	A3	20051128		
JP 2003506366	T	20030218	JP 2001-514316	20000802
AT 241611	T	20030615	AT 2000-949831	20000802
PT 1206462	T	20031031	PT 2000-949831	20000802
ES 2200900	T3	20040316	ES 2000-949831	20000802
AU 772206	B2	20040422	AU 2000-63090	20000802
NZ 517422	A	20050225	NZ 2000-517422	20000802
RU 2247723	C2	20050310	RU 2002-105518	20000802
AP 1383	A	20050405	AP 2002-2413	20000802
NO 2002000485	A	20020321	NO 2002-485	20020130
ZA 2002000838	A	20030605	ZA 2002-838	20020130
IN 2002CN00148	A	20050311	IN 2002-CN148	20020130
BG 106373	A	20020930	BG 2002-106373	20020131
MX 2002PA01117	A	20030820	MX 2002-PA1117	20020131
HR 2002000103	B1	20050630	HR 2002-103	20020201
US 6815465	B1	20041109	US 2002-48659	20020603
HK 1048995	A1	20060721	HK 2003-101165	20030218
PRIORITY APPLN. INFO.:			HU 1999-2628	A 19990802
			WO 2000-HU88	W 20000802

OTHER SOURCE(S): MARPAT 134:147437

GI



AB Borrelidin derivs., such as I [R = -COOR₁, -CONR₂R₃, -CONR₄CONR₄R₅ or -CH₂OR₆; R₁ = alkyl, cycloalkyl; R₂, R₃ = H, alkyl, cycloalkyl, heteroaryl; R₄, R₅ = H, alkyl, cycloalkyl, phenyl; R₆ = H, alkyl, cycloalkyl, Ph, carbamoyl, benzoyl, alkylsulfonyl], were prepared to inhibit the neovascularization in living tissues and as such can be used for preventing and inhibiting angiogenesis appearing in connection with tumor growth and for preventing the formation of tumor metastases. Thus, I [R = -CO₂(CH₂)₂R₁, R₁ = 4-morpholinyl] was prepared by esterifying borrelidin with 4-(2-hydroxyethyl)morpholine using 1-hydroxybenzotriazole, 4-dimethylaminopyridine and dicyclohexylcarbodiimide in THF. The prepared borrelidin derivs. were tested for angiogenesis inhibiting activity.

IT 7184-60-3, Borrelidin

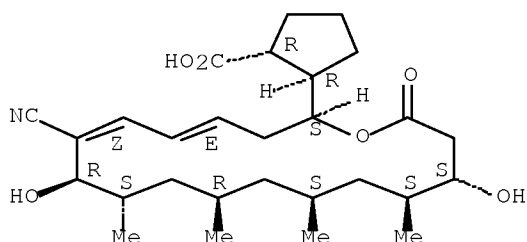
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of borrelidin derivs. for pharmaceutical use as angiogenesis inhibiting agents)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM C07D313-00

ICS C07D405-12; A61K031-335; A61P035-00

CC 26-6 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1

IT 100-46-9, Benzenemethanamine, reactions 103-74-2, 2-Pyridineethanol
108-91-8, Cyclohexanamine, reactions 141-43-5, reactions 462-08-8,
3-Pyridinamine 617-89-0, 2-Furanmethanamine 622-40-2,
4-Morpholineethanol 2038-03-1, 4-Morpholineethanamine 2387-23-7
3731-51-9, 2-Pyridinemethanamine 3731-52-0, 3-Pyridinemethanamine

10/534210

3731-53-1, 4-Pyridinemethanamine 7184-60-3, Borrelidin
27532-96-3

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of borrelidin derivs. for pharmaceutical use as angiogenesis
inhibiting agents)

L45 ANSWER 17 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:106028 HCAPLUS Full-text

DOCUMENT NUMBER: 128:179453

ORIGINAL REFERENCE NO.: 128:35415a,35418a

TITLE: Novel strains of Escherichia coli containing
recombinant plasmids for improved production of
L-threonine by fermentation

INVENTOR(S): Wang, Ming-Der; Bradshaw, Jill S.; Swisher, Stacia L.;
Liaw, Hungming James; Hanke, Paul D.; Binder, Thomas
P.

PATENT ASSIGNEE(S): Archer-Daniels-Midland Company, USA

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804715	A1	19980205	WO 1997-US13359	19970730
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5939307	A	19990817	US 1997-902336	19970729
CA 2262813	A1	19980205	CA 1997-2262813	19970730
ZA 9706803	A	19980219	ZA 1997-6803	19970730
AU 9738994	A	19980220	AU 1997-38994	19970730
AU 730102	B2	20010222		
EP 917578	A1	19990526	EP 1997-936291	19970730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1226931	A	19990825	CN 1997-196897	19970730
BR 9710503	A	20000111	BR 1997-10503	19970730
HU 9903856	A2	20000328	HU 1999-3856	19970730
NZ 334032	A	20000929	NZ 1997-334032	19970730
JP 2000515763	T	20001128	JP 1998-509111	19970730
RU 2212448	C2	20030920	RU 1999-104488	19970730
PL 191395	B1	20060531	PL 1997-331351	19970730
NO 9900362	A	19990126	NO 1999-362	19990126
NO 320044	B1	20051017		
KR 2000029691	A	20000525	KR 1999-700770	19990129
PRIORITY APPLN. INFO.:			US 1996-22407P	P 19960730
			WO 1997-US13359	W 19970730

AB Disclosed is a strain of Escherichia coli containing in its chromosome a
genetic determinant of amino acid biosynthesis, e.g., the threonine operon,
under the control of a non-native promoter for the production of threonine.
It does not require any recombinant plasmids containing genes that encode
threonine biosynthetic enzymes to produce threonine. Optionally, amino acid

10/534210

nutritional requirements for and/or regulatory hindrance to amino acid biosynthesis are removed from the chromosome. Preparation of Escherichia coli strains containing the threonine operon from E. coli strain ATCC 21277, the tac promoter, a defective threonine dehydrogenase gene, borrelidin resistance, etc. was demonstrated. Escherichia coli strain kat-13 produced 102 threonine g/L after 48-h fermentation

IT 7184-60-3, Borrelidin

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(resistance to; threonine high producer Escherichia coli strain containing in chromosome; novel strains of Escherichia coli without containing recombinant plasmids for improved production of L-threonine by

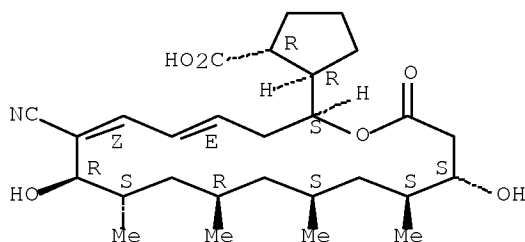
fermentation)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IC ICM C12N015-52

ICS C12P013-08; C12N015-70; C12N015-90; C12N001-21; C12N001-21; C12R001-19

CC 16-2 (Fermentation and Bioindustrial Chemistry)

Section cross-reference(s): 10

IT 7184-60-3, Borrelidin

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(resistance to; threonine high producer Escherichia coli strain containing in chromosome; novel strains of Escherichia coli without containing recombinant plasmids for improved production of L-threonine by

fermentation)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1993:441918 HCAPLUS Full-text

DOCUMENT NUMBER: 119:41918

ORIGINAL REFERENCE NO.: 119:7483a, 7486a

TITLE: Threonyl-tRNA synthetase gene amplification in borrelidin-resistant mammalian cells

AUTHOR(S): Arfin, Stuart M.; Gerken, Steven C.; Kontis, Kris J.; Cruzen, Matt E.

CORPORATE SOURCE: Univ. California, Irvine, CA, USA

SOURCE: Gene Amplif. Mamm. Cells (1993), 97-106. Editor(s): Kellems, Rodney E. Dekker: New York, N. Y.

CODEN: 58VCAS

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review with 15 refs on threonyl-tRNA synthetase gene amplification in response to the antibiotic borrelidin. Topics include: selection of borrelidin-resistant chinese hamster ovary cells; threonyl-tRNA synthetase activity, protein and mRNA levels, and gene copy number; regulation of threonyl-tRNA synthetase expression; and preliminary characterization of the threonyl-tRNA synthetase gene.

IT 7184-60-3, Borrelidin

RL: BIOL (Biological study)

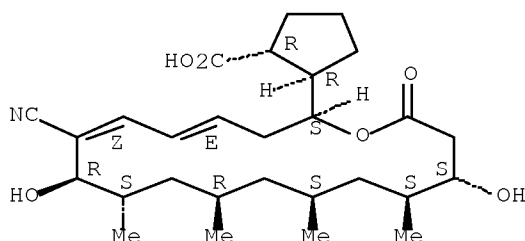
(resistance to, threonyl-tRNA synthetase gene amplification for)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



CC 3-0 (Biochemical Genetics)

Section cross-reference(s): 1

IT 7184-60-3, Borrelidin

RL: BIOL (Biological study)

(resistance to, threonyl-tRNA synthetase gene amplification for)

L45 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1992:52826 HCAPLUS Full-text

DOCUMENT NUMBER: 116:52826

ORIGINAL REFERENCE NO.: 116:9015a,9018a

TITLE: Four major transcriptional responses in the methionine/threonine biosynthetic pathway of *Saccharomyces cerevisiae*

AUTHOR(S): Mountain, Harry A.; Bystroem, Anders S.; Larsen, Joergen Tang; Korch, Christopher

CORPORATE SOURCE: Dep. Microbiol., Univ. Umea, Umea, S-901 87, Swed.

SOURCE: Yeast (1991), 7(8), 781-803

CODEN: YESTE3; ISSN: 0749-503X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Genes encoding enzymes in the threonine/methionine biosynthetic pathway were cloned and used to investigate their transcriptional response to signals known to affect gene expression on the basis of enzyme specific-activities. Four major responses were evident: strong repression by methionine of MET3, MET5 and MET14, as previously described for MET3, MET2 and MET25; weak repression by methionine of MET6; weak stimulation by methionine but no response to threonine was seen for THR1, HOM2 and HOM3; no response to any of the signals

tested, for HOM6 and MES1. In a BOR3 mutant, THR1, HOM2 and HOM3 mRNA levels were increased slightly. The stimulation of transcription by methionine for HOM2, HOM3 and THR1 is mediated by the GCN4 gene product and hence these genes are under the general amino acid control. In addition to the strong repression by methionine, MET5 is also regulated by the general control.

IT 7184-60-3, Borrelidin

RL: BIOL (Biological study)

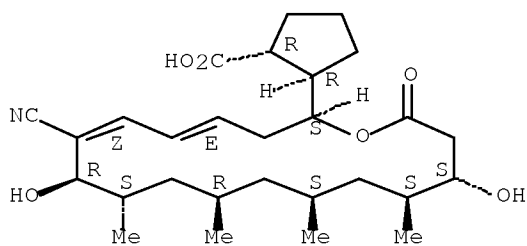
(BOR genes for resistance to, of *Saccharomyces cerevisiae*,
methionine/threonine biosynthesis regulation in relation to)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



CC 3-4 (Biochemical Genetics)

Section cross-reference(s): 10

IT *Saccharomyces cerevisiae*

(methionine/threonine biosynthesis genes of,
transcription of)

IT Transcription, genetic

(of methionine/threonine biosynthesis genes of,
Saccharomyces cerevisiae)

IT Molecular cloning

(of methionine/threonine biosynthetic pathway genes, of
Saccharomyces cerevisiae)

IT Genetic mapping

(restriction endonuclease, of methionine/threonine biosynthetic
pathway genes, of yeast)

IT 7184-60-3, Borrelidin

RL: BIOL (Biological study)

(BOR genes for resistance to, of *Saccharomyces cerevisiae*,
methionine/threonine biosynthesis regulation in relation to)

L45 ANSWER 20 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1989:402086 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 111:2086

ORIGINAL REFERENCE NO.: 111:411a, 414a

TITLE: Isolation of a cDNA clone for human threonyl-tRNA
synthetase: amplification of the structural gene in
borrelidin-resistant cell lines

AUTHOR(S): Kontis, Kris J.; Arfin, Stuart M.

CORPORATE SOURCE: Coll. Med., Univ. California, Irvine, CA, 92717, USA

SOURCE: Molecular and Cellular Biology (1989), 9(5), 1832-8
CODEN: MCEBD4; ISSN: 0270-7306

DOCUMENT TYPE: Journal
 LANGUAGE: English

AB A cDNA for threonyl-tRNA synthetase was isolated from a human placental cDNA λ gt11 expression library by immunol. screening, and its identity was confirmed by hybrid-selected mRNA translation. With this cDNA used as a hybridization probe, borrelidin-resistant Chinese hamster ovary cells that overproduced threonyl-tRNA synthetase were shown to have increased levels of threonyl-tRNA synthetase mRNA and gene sequences. Amplification of the gene did not appear to have been accompanied by any major structural reorganizations.

IT 7184-60-3, Borrelidin

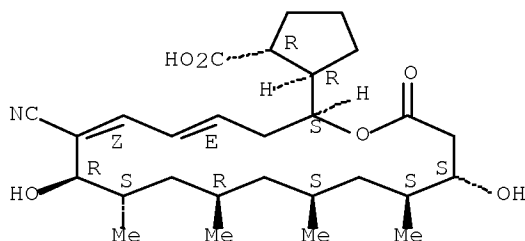
RL: PRP (Properties)

(CHO cells resistant to, human threonyl-tRNA synthetase mRNA formation in)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



CC 3-4 (Biochemical Genetics)
 Section cross-reference(s): 13

IT 7184-60-3, Borrelidin

RL: PRP (Properties)

(CHO cells resistant to, human threonyl-tRNA synthetase mRNA formation in)

L45 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:450922 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 103:50922

ORIGINAL REFERENCE NO.: 103:8151a,8154a

TITLE: Treponemycin, a nitrile antibiotic active against *Treponema hyodysenteriae*

AUTHOR(S): Singh, S. K.; Gurusiddaiah, S.; Whalen, J. W.

CORPORATE SOURCE: Bioanal. Cent., Washington State Univ., Pullman, WA, 99164, USA

SOURCE: Antimicrobial Agents and Chemotherapy (1985), 27(2), 239-45

CODEN: AMACQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two strains of *Streptomyces* (isolates 275 and 124) were isolated from soil samples. Based on their cellular morphol. and physiol., the 2 isolates were identified as *S. albovinaceus*. Both isolates produced an antibiotic when grown in liquid culture medium containing homogenized oats. The antibiotic, treponemycin (I), was isolated from the culture broth by solvent extraction

and purified by silica gel column and preparative TLC. I is a crystalline light-yellow compound, m.p. 93-5°, that is levorotatory and soluble in most organic solvents. It is sparingly soluble in water but insol. in petroleum ether. On the basis of elemental anal. and mass spectral data, its mol. formula was deduced to be C₂₈H₄₃O₆N. IR spectra indicated the presence of unsatn., nitrile, lactone, ester, or all 3 functions, and carbonyl functions in I. A sharp IR absorption band for nitrile at 2220 cm⁻¹ and the presence of an unsatd. group indicated that the nitrile function may be attached to an unsatd. C atom. The presence of dienenitrile functions was further supported by the UV absorption spectrum of the antibiotic, which gave a UV_{max} at 257 nm. The NMR spectrum did not give any peak which could be exchanged with D₂O, an indication of the absence of carboxylic and hydroxyl functions in I. All of the functional groupings indicated by the IR and UV spectra were further confirmed by the ¹³C-NMR spectrum. A brief hydrogenation of I yielded a biol. active tetrahydro derivative, whereas extended hydrogenation produced an inactive primary amine. Mild alkaline hydrolysis and subsequent esterification of the antibiotic with diazomethane produced an inactive di-Me ester. Apparently both the nitrile and the lactone functions are essential for I to show antimicrobial activity. I inhibited several species of bacteria, especially *T. hyodysenteriae*, the causative agent of swine dysentery. In view of the oral 50% LD of 400 mg/kg and its low min. inhibitory concentration against 4 strains of *T. hyodysenteriae*, I may have value as a swine dysentery therapeutic.

IT 7184-60-3

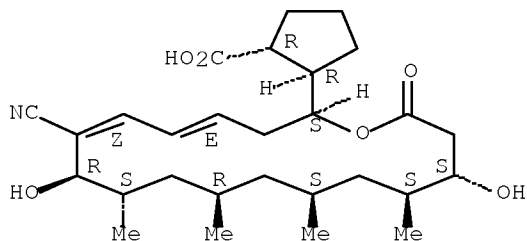
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(from *Streptomyces albobovineus*, anti- *Treponema hyodysenteriae* activity of)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



CC 10-1 (Microbial Biochemistry)

Section cross-reference(s): 1

IT 7184-60-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(from *Streptomyces albobovineus*, anti- *Treponema hyodysenteriae* activity of)

L45 ANSWER 22 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1975:437367 HCAPLUS Full-text

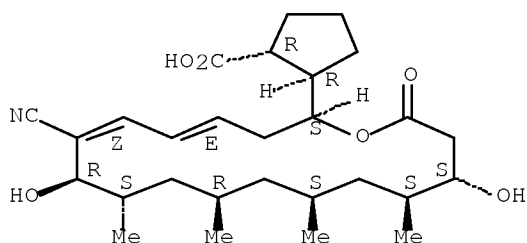
DOCUMENT NUMBER: 83:37367

ORIGINAL REFERENCE NO.: 83:5859a,5862a
 TITLE: Borrelidin
 AUTHOR(S): Poralla, K.
 CORPORATE SOURCE: Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.
 SOURCE: Antibiotics (1975), Volume 3, 365-9. Editor(s):
 Gottlieb, David; Shaw, Paul D.; Corcoran, John W.
 Springer: New York, N. Y.
 CODEN: 19SYA8

DOCUMENT TYPE: Conference; General Review
 LANGUAGE: English

GI For diagram(s), see printed CA Issue.
 AB A review with 19 refs. discussing the antibiotic activity of borrelidin (I)
 [7184-60-3].
 IT 7184-60-3
 RL: BIOL (Biological study)
 RN 7184-60-3 HCAPLUS
 CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-
 8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-
 yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



CC 1-0 (Pharmacodynamics)
 Section cross-reference(s): 3
 IT 7184-60-3
 RL: BIOL (Biological study)

L45 ANSWER 23 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1974:433850 HCAPLUS Full-text

DOCUMENT NUMBER: 81:33850

ORIGINAL REFERENCE NO.: 81:5412h,5413a

TITLE: Microbial production of L-threonine. IV. Effect of
 the antibiotic, borrelidin, on the production of
 L-threonine by Escherichia coli auxotrophs

AUTHOR(S): Hirakawa, Tamotsu; Morinaga, Haruhiko; Watanabe,
 Kiyoshi

CORPORATE SOURCE: Biochem. Res. Lab., Kanegafuchi Chem. Ind. Co., Ltd.,
 Takasago, Japan

SOURCE: Agricultural and Biological Chemistry (1974), 38(1),
 85-9

CODEN: ABCHA6; ISSN: 0002-1369

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Borrelidin (I) [7184-60-3] greatly increased formation of L-threonine [72-19-
 5] by all 4 E. coli auxotrophs studied. Maximum yield of L-threonine (6.4
 mg/ml) was observed with strain number 15 in the presence of 10 µg I/ml.

Sodium L-aspartate [17090-93-6] enhanced the effect of I on L-threonine formation. The maximum amount of L-threonine formed by E. coli strain number 234 in the presence of 5 mg sodium aspartate/ml and 10 µg I/ml was 50.0 mg/ml.

IT 7184-60-3

RL: PRP (Properties)

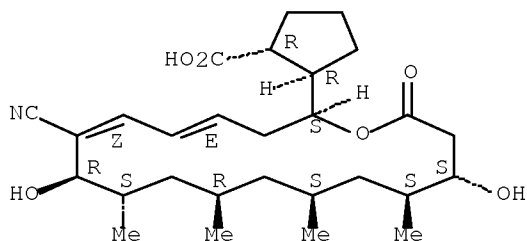
(threonine fermentation enhancement by, in Escherichia coli)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



CC 3-2 (Biochemical Interactions)

Section cross-reference(s): 16

IT 7184-60-3

RL: PRP (Properties)

(threonine fermentation enhancement by, in Escherichia coli)

L45 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1974:66945 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 80:66945

ORIGINAL REFERENCE NO.: 80:10819a,10822a

TITLE: Electron-optical investigation of the effect of streptomycete's antibiotic borrelidin on the Pseudorabies virus

AUTHOR(S): Zoepel, P.; Eckardt, K.; Tonew, E. M.

CORPORATE SOURCE: Forschungszent. Molekularbiol. Med., Akad. Wiss., Jena, Ger. Dem. Rep.

SOURCE: Zeitschrift fuer Allgemeine Mikrobiologie (1973), 13(8), 711-22

CODEN: ZAPOAK; ISSN: 0044-2208

DOCUMENT TYPE: Journal

LANGUAGE: German

AB Electron micrographs of Pseudorabies virus replication in borrelidin (I) [7184-60-3] (2 and 5 µg/ml)-treated chicken embryonal fibroblasts (CEF) revealed an effect of I on the early steps of viral replication. Incomplete viral particles were found in the cytoplasm of I-treated CEF at a time when the regular viral replication cycle was finished in untreated control CEF. The antiviral activity of I probably depended on a blockade of the virus specific protein synthesis.

IT 7184-60-3

RL: PRP (Properties)

(pseudorabies virus replication inhibition by)

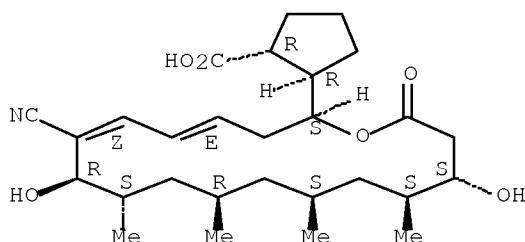
RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-

10/534210

8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 3-2 (Biochemical Interactions)
IT 7184-60-3
RL: PRP (Properties)
(pseudorabies virus replication inhibition by)

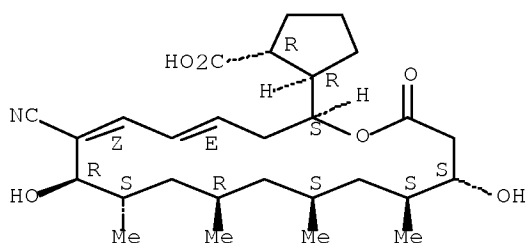
L45 ANSWER 25 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1970:411565 HCAPLUS Full-text
DOCUMENT NUMBER: 73:11565
ORIGINAL REFERENCE NO.: 73:1917a,1920a
TITLE: Effect of borrelidin on the protein biosynthesis and the regulatory process in microorganisms
AUTHOR(S): Nass, Gisela
CORPORATE SOURCE: Max-Planck-Inst. Mol.-Genet., Berlin, Fed. Rep. Ger.
SOURCE: Zentralblatt fuer Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene, Abteilung 1: Medizinisch-Hygienische Bakteriologie, Virusforschung und Parasitologie, Originale (1970), 212(2-4), 239-45
CODEN: ZBPHA6; ISSN: 0372-8110
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The antibiotic borrelidin (I) inhibits the enzymic activity of threonyl-tRNA synthetase (II) in Escherichia coli and yeast. Besides the inhibition of protein biosynthesis the action of I leads to a derepression of the formation of the threonine-biosynthetic enzymes in these cells, indicating that in single celled organisms (E. coli) as well as in more complex single celled organisms (yeast) II takes part in the repression of the threonine biosynthetic enzymes. The altered II activity in I-resistant E. coli mutants demonstrates the action of I on II.

IT 7184-60-3
RL: BIOL (Biological study)
(threonine formation derepression by, in microorganisms)

RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 8 (Microbial Biochemistry)

IT 7184-60-3

RL: BIOL (Biological study)

(threonine formation derepression by, in microorganisms)

L45 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1968:103621 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 68:103621

ORIGINAL REFERENCE NO.: 68:19987a,19990a

TITLE: Metabolic products of microorganisms. LXII.

Inhibition of the attachment of threonine to sRNA in a cell-free system and of the synthesis of protein and nucleic acids in the cell by the antibiotic borrelidin

AUTHOR(S): Poralla, K.; Zaehner, Hans

CORPORATE SOURCE: Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.

SOURCE: Archiv fuer Mikrobiologie (1968), 61, 143-53

CODEN: ARMKA7; ISSN: 0003-9276

DOCUMENT TYPE: Journal

LANGUAGE: German

AB Borrelidin specifically inhibited the attachment of L-threonine to soluble RNA at a concentration of 1.4×10^{-6} M in a cell-free system of *Bacillus subtilis*. It did not inhibit the incorporation of L-isoleucine, L-valine, L-tyrosine, L-serine, L-glutamic acid, or L-proline. The macrolide antibiotics, lankamycin and erythromycin, at concns. 10-fold greater than required to inhibit growth, did not inhibit the binding of L-threonine or other amino acids to soluble RNA. In the cells, borrelidin (1.5×10^{-6} M) inhibited the synthesis of protein, RNA, and DNA. Lankamycin and erythromycin selectively inhibited protein synthesis. Borrelidin is the first antibiotic known to block protein synthesis via inhibition of the incorporation of amino acids into soluble RNA. 32 references.

IT 7184-60-3

RL: BIOL (Biological study)

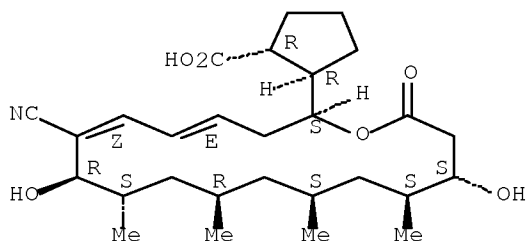
(inhibition of nucleic acids and protein formation by, in *Bacillus subtilis*)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



CC 15 (Pharmacodynamics)

IT 7184-60-3

RL: BIOL (Biological study)

(inhibition of nucleic acids and protein formation by, in *Bacillus subtilis*)

L45 ANSWER 27 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1965:405847 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 63:5847

ORIGINAL REFERENCE NO.: 63:1078b-d

TITLE: Antiviral activity of two antibiotics isolated from a species of *Streptomyces*

AUTHOR(S): Dickinson, Lois; Griffiths, A. J.; Mason, C. G.; Mills, R. F. N.

CORPORATE SOURCE: Boots Pure Drug Co., Ltd., Nottingham, UK

SOURCE: Nature (London, United Kingdom) (1965), 206(4981), 265-8

CODEN: NATUAS; ISSN: 0028-0836

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Antiviral activity was shown against influenza virus, Newcastle disease virus, and vaccinia virus growing in chick embryo monolayers and against encephalomyocarditis virus growing in suspensions of Kreb's ascites tumor cells by liquors from *Streptomyces* C2989, but the liquors were inactive against bacteria. One of the liquors was injected intraperitoneally or subcutaneously into mice infected with encephalomyocarditis virus and found to markedly increase the number of animals that survived for 10 days. Borrelidin was found to be the inhibitor of in vitro virus growth, but it had no effect on the in vivo virus infections in mice. Another liquor from the culture of *Streptomyces* C2989 yielded vivomycin which was effective against the in vivo infections of encephalomyocarditis virus in mice if it was given intraperitoneally, intranasally, or subcutaneously, but not orally or intracerebrally. There was a synergistic effect obtained when vivomycin was given with borrelidin to mice infected with encephalomyocarditis virus or ascites tumor (against which neither had much activity alone) and against influenza virus in eggs. Vivomycin stimulated host defense mechanisms in a manner similar to that of endotoxins and like them is less toxic to mice than to dogs and rabbits.

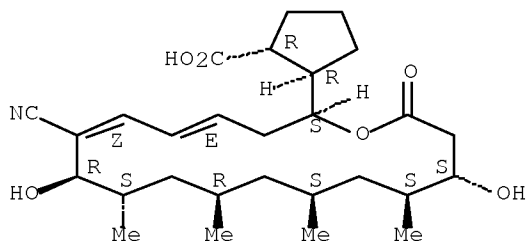
IT 7184-60-3, Borrelidin
(as virucide)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



CC 68 (Pharmacodynamics)
 IT 7184-60-3, Borrelidin
 (as virucide)

L45 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1965:430867 HCAPLUS Full-text

DOCUMENT NUMBER: 63:30867

ORIGINAL REFERENCE NO.: 63:5448c-f

TITLE: Isolation of vivomycin and borrelidin, two antibiotics with antiviral activity, from a species of *Streptomyces*

AUTHOR(S): Lumb, M.; Macey, P. E.; Spyvee, J.; Whitmarsh, J. M.; Wright, R. D.

CORPORATE SOURCE: Boots Pure Drug Co., Ltd., Nottingham, UK

SOURCE: Nature (London, United Kingdom) (1965), 206(4981), 263-5

CODEN: NATUAS; ISSN: 0028-0836

DOCUMENT TYPE: Journal

LANGUAGE: English

AB cf. Dickinson, et al., CA 63, 1078b. Both antibacterial (especially against *Corynebacterium*) and antiviral activity was exhibited by the culture fluid of the organism. Maximum activity was reached after 96 hrs. of cultivation. The 1st antibiotic was found to be borrelidin (I) (Berger, et al., CA 44, 697a). It was extracted from culture fluids with BuOH or Me iso-Bu ketone, concentrated under vacuum, stirred with MeOH, decanted from the insol. fat, again concentrated under vacuum and precipitated with light petroleum to give 0.5 g./l. of broth, 10-20% pure. This material had high activity against *C. xerosis* and viruses in vitro, but no activity against encephalomyocarditis (EMC) virus in mice. The crude I (absolute maximum at 258 mμ) was concentrated by countercurrent extraction in water-MeOH-Me iso-Bu ketone-ligroine (5:5:2:8). Concentration and precipitation gave a colorless solid, m. 98-105°, containing 640 units/mg. It crystallized to colorless hexagonal plates from CHCl₃-CCl₄. The waste aqueous liquors contained another antibiotic, active in vivo but not in vitro. It was called vivomycin (II). It was produced maximally in the same culture after 48-60 hrs. incubation. I remaining in the broth was partially removed by acidifying to pH 2 and filtering; the remaining I was removed by washing with BuOH or Me iso-Bu ketone, or by absorbing the I and II from the neutralized liquor onto charcoal and eluting the II with 50% aqueous acetone. The crude solid II could be separated into a number of components by thin-layer chromatography with BuOH-HOAc-H₂O (12:3:5) and tert-BuOH-HOAc-H₂O (8:2:5). The most active component remained at the origin in the latter solvent. Purification on columns of G-25 and G-75 Sephadex gave a fibrous white solid, active against EMC virus in mice at 0.4-1.5 mg./kg. It appeared to be a polysaccharide containing about 48-55% arabinose, 16-21% galactose, and 22-31% glucose.

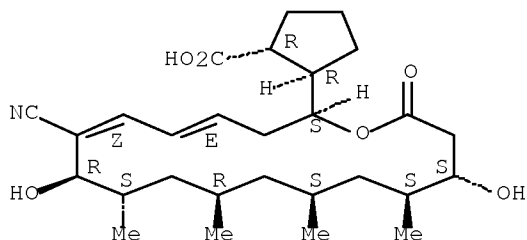
IT 7184-60-3P, Borrelidin

RL: PREP (Preparation)
(separation from vivomycin)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 30 (Pharmaceuticals)
IT 7184-60-3P, Borrelidin
RL: PREP (Preparation)
(separation from vivomycin)

L45 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1954:50462 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 48:50462

ORIGINAL REFERENCE NO.: 48:8966b-d

TITLE: The effect of antibiotics upon the growth of Sarcoma 180 in vivo

AUTHOR(S): Reilly, H. Christine; Stock, C. Chester; Buckley, Sonja M.; Clark, Donald A.

CORPORATE SOURCE: Sloan-Kettering Inst. for Cancer Research, New York, NY

SOURCE: Cancer Research (1953), 13, 684-7
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Actidione, actinomycin, illudin M, illudin S, and terramycin slightly retarded the growth of Crocker Sarcoma 180 in mice. With the latter 4, tumor was retarded only at doses toxic for the host. None of these compds. gave as marked effects on the development of the tumor as was previously observed with the basic protein preparation from *Aspergillus fumigatus*, the folic acid analogs, 6-mercaptopurine, or 2,4,6-triethylenimino-s-triazine. No tumor retardation was exhibited by aerosporin (Polymyxin B), antimycin A, aspergillilic acid, Aureomycin, bacitracin, borrelidin (Na salt), candicidin, chloromycetin, circulin-HCl, citrinin, cordycepin, dihydrostreptomycin sulfate fumagillin, crude fungicidin, gliotoxin, gramicidin, neomycin, netropsin (-HCl or sulfate), phagopedin sigma (Na salt), polypeptin, rimocidin, streptomycin sulfate, streptothricin-HCl, subtilin, tyrocidine-HCl, tyrothricin, viomycin, and viscosin. Of more than 1200 crude antibiotic prepns. tested, 5 caused sufficient tumor retardation to be considered for further work.

IT 7184-60-3, Borrelidin
(effect on sarcoma growth)

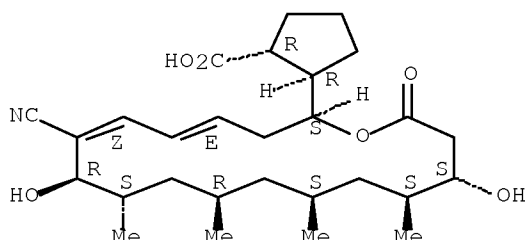
RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-

10/534210

8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 11H (Biological Chemistry: Pharmacology)
IT 50-44-2, 6-Purinethiol 56-75-7, Chloramphenicol 57-62-5,
Chlortetracycline 57-92-1, Streptomycin 66-81-9, Glutarimide,
3-[2-(3,5-dimethyl-2-oxocyclohexyl-2-hydroxyethyl)]- 67-99-2, Gliotoxin
73-03-0, Cordycepin 79-57-2, Oxytetracycline 490-02-8, Aspergillic
acid 518-75-2, Citrinin 1146-04-9, Illudin M 1149-99-1, Illudin S
1393-12-0, Rimocidin 1393-38-0, Subtilin 1397-94-0, Antimycin A
1400-61-9, Nystatin 1402-38-6, Actinomycins 1403-17-4, Candicidin
1404-04-2, Neomycin 1404-32-6, Polypeptin 1404-88-2, Tyrothricin
1405-87-4, Bacitracin 7184-60-3, Borrelidin 8011-61-8,
Tyrocidine 9008-54-2, Circulin 23110-15-8, Fumagillin 27127-62-4,
Viscosin 32988-50-4, Viomycin
(effect on sarcoma growth)

L45 ANSWER 30 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1951:19784 HCAPLUS Full-text

DOCUMENT NUMBER: 45:19784

ORIGINAL REFERENCE NO.: 45:3505f-h

TITLE: Effect of niacin and tryptophan in counteracting
toxicity of crystalline borrelidin for the rat

AUTHOR(S): Cooperman, J. M.; Rubin, S. H.; Tabenkin, B.

CORPORATE SOURCE: Hoffmann-La Roche Co., Nutley, NJ

SOURCE: Proceedings of the Society for Experimental Biology
and Medicine (1951), 76, 18-20
CODEN: PSEBAA; ISSN: 0037-9727

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

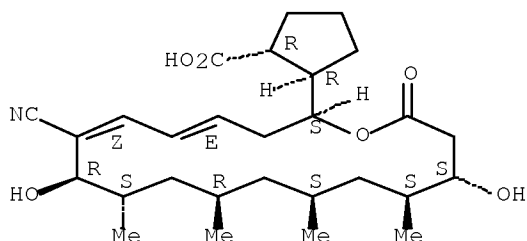
AB When the crystalline antibiotic borrelidin (cf. C.A. 44, 697a) was given
orally to rats, 2 γ /day had no effect on the growth rate, 10 γ /day retarded
growth, and 20 γ /day resulted in a high mortality rate. The inhibition of
growth by 10 γ /day was partially counteracted by supplementation with niacin.
Poor growth was also obtained by adding 1-2 mg./kg. of borrelidin to the stock
ration. This effect was partially overcome by feeding extra niacin or
tryptophan.

IT 7184-60-3, Borrelidin
(toxicity of, effect of niacin and tryptophan on)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-
8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-
yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 11H (Biological Chemistry: Pharmacology)
IT 7184-60-3, Borrelidin
(toxicity of, effect of niacin and tryptophan on)

L45 ANSWER 31 OF 40 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004287561 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15186422
TITLE: Biosynthesis of the angiogenesis inhibitor borrelidin by *Streptomyces parvulus* Tu4055: insights into nitrile formation.
AUTHOR: Olano Carlos; Moss Steven J; Brana Alfredo F; Sheridan Rose M; Math Vidya; Weston Alison J; Mendez Carmen; Leadlay Peter F; Wilkinson Barrie; Salas Jose A
CORPORATE SOURCE: Departamento de Biología Funcional e Instituto Universitario de Oncología del Principado de Asturias, Universidad de Oviedo, 33006 Oviedo, Spain.
SOURCE: Molecular microbiology, (2004 Jun) Vol. 52, No. 6, pp. 1745-56.
Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 10 Jun 2004
Last Updated on STN: 2 Feb 2005
Entered Medline: 31 Jan 2005
AB The 18-membered polyketide macrolide borrelidin exhibits a number of important biological activities, including potent angiogenesis inhibition. This has prompted two recent total syntheses as well as the cloning of the biosynthetic gene cluster from *Streptomyces parvulus* Tu4055. Borrelidin possesses some unusual structural characteristics, including a cyclopentane carboxylic acid moiety at C17 and a nitrile moiety at C12 of the macrocyclic ring. Nitrile groups are relatively rare in nature, and little is known of their biosynthesis during secondary metabolism. The nitrile group of borrelidin is shown here to arise from the methyl group of a methylmalonyl-CoA extender unit incorporated during polyketide chain extension. Insertional inactivation of two genes in the borrelidin gene cluster, *borI* (coding for a cytochrome P450 monooxygenase) and *borJ* (coding for an aminotransferase), generated borrelidin non-producing mutants. These mutants accumulated different compounds lacking

the C12 nitrile moiety, with the product of the borI-minus mutant (12-desnitrile-12-methyl-borrelidin) possessing a methyl group and that of the borJ-minus mutant (12-desnitrile-12-carboxyl-borrelidin) a carboxyl group at C12. The former but not the latter was converted into borrelidin when biotransformed by an *S. parvulus* mutant that is deficient in the biosynthesis of the borrelidin starter unit. This suggests that 12-desnitrile-12-methyl-borrelidin is a competent biosynthetic intermediate, whereas the carboxylated derivative is a shunt metabolite. Bioconversion of 12-desnitrile-12-methyl-borrelidin into borrelidin was also achieved in a heterologous system co-expressing borI and borJ in *Streptomyces albus* J1074. This bioconversion was more efficient when borK, which is believed to encode a dehydrogenase, was simultaneously expressed with borI and borJ. On the basis of these findings, a pathway is proposed for the formation of the nitrile moiety during borrelidin biosynthesis.

CT Acyl Coenzyme A: ME, metabolism
 Bacterial Proteins: GE, genetics
 Bacterial Proteins: ME, metabolism
 Biotransformation
 Cloning, Molecular
 *Fatty Alcohols: CH, chemistry
 *Fatty Alcohols: ME, metabolism
 Genes, Bacterial
 Mixed Function Oxygenases: GE, genetics
 Mixed Function Oxygenases: ME, metabolism
 Mutagenesis, Insertional
 Mutation
 *Nitriles: CH, chemistry
 *Nitriles: ME, metabolism
 Oxidoreductases: GE, genetics
 Oxidoreductases: ME, metabolism
 Recombinant Proteins: GE, genetics
 Recombinant Proteins: ME, metabolism
 Streptomyces: GE, genetics
 *Streptomyces: ME, metabolism
 Transaminases: GE, genetics
 Transaminases: ME, metabolism
 RN 1264-45-5 (methylmalonyl-coenzyme A); 7184-60-3 (borrelidin)
 CN 0 (Acyl Coenzyme A); 0 (Bacterial Proteins); 0 (Fatty Alcohols); 0 (Nitriles); 0 (Recombinant Proteins); EC 1.- (Mixed Function Oxygenases); EC 1.- (Oxidoreductases); EC 2.6.1.- (Transaminases)

L45 ANSWER 32 OF 40 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 2004215134 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 15112998
 TITLE: Biosynthesis of the angiogenesis inhibitor borrelidin by *Streptomyces parvulus* Tu4055: cluster analysis and assignment of functions.
 AUTHOR: Olano Carlos; Wilkinson Barrie; Sanchez Cesar; Moss Steven J; Sheridan Rose; Math Vidya; Weston Alison J; Brana Alfredo F; Martin Christine J; Oliynyk Markiyana; Mendez Carmen; Leadlay Peter F; Salas Jose A
 CORPORATE SOURCE: Departamento de Biología Funcional e Instituto Universitario de Oncología del Principado de Asturias, Universidad de Oviedo, 33006 Oviedo, Spain.
 SOURCE: Chemistry & biology, (2004 Jan) Vol. 11, No. 1, pp. 87-97. Journal code: 9500160. ISSN: 1074-5521.
 PUB. COUNTRY: England: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English

FILE SEGMENT: Priority Journals
 OTHER SOURCE: GENBANK-AB070949; GENBANK-AF237573; GENBANK-AJ002571;
 GENBANK-AJ580915; GENBANK-AY045929
 ENTRY MONTH: 200409
 ENTRY DATE: Entered STN: 29 Apr 2004
 Last Updated on STN: 1 Oct 2004
 Entered Medline: 30 Sep 2004

AB The biosynthetic gene cluster for the angiogenesis inhibitor borrelidin has been cloned from *Streptomyces parvulus* Tu4055. Sequence analysis indicates that the macrolide ring of borrelidin is formed by a modular polyketide synthase (PKS) (borA1-A6), a result that was confirmed by disruption of borA3. The borrelidin PKS is striking because only seven rather than the nine modules expected for a nonaketide product are encoded by borA1-A6. The starter unit of the PKS has been verified as trans-cyclopentane-1,2-dicarboxylic acid (trans-1,2-CPDA), and the genes involved in its biosynthesis identified. Other genes responsible for biosynthesis of the nitrile moiety, regulation, and self-resistance were also identified.

CT *Angiogenesis Inhibitors: BI, biosynthesis
 Angiogenesis Inhibitors: CH, chemistry
 Cloning, Molecular
 Cyclopentanes: CS, chemical synthesis
 Dicarboxylic Acids: CS, chemical synthesis
 Fatty Alcohols: CH, chemistry
 *Fatty Alcohols: ME, metabolism
 *Genes, Bacterial
 Models, Chemical
 Molecular Sequence Data
 Molecular Structure
 Multienzyme Complexes: GE, genetics
 *Multigene Family
 Sequence Analysis, DNA
 Streptomyces: EN, enzymology
 *Streptomyces: GE, genetics
 Streptomyces: ME, metabolism

RN 7184-60-3 (borrelidin)

CN 0 (Angiogenesis Inhibitors); 0 (Cyclopentanes); 0 (Dicarboxylic Acids); 0 (Fatty Alcohols); 0 (Multienzyme Complexes)

L45 ANSWER 33 OF 40 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:80646 BIOSIS Full-text
 DOCUMENT NUMBER: PREV200600076587
 TITLE: Biosynthetic studies of the angiogenesis inhibitor borrelidin.
 AUTHOR(S): Wilkinson, Barrie [Reprint Author]; Moss, Steven J.; Olano, Carlos; Brana, Alfredo F.; Sheridan, Rose M.; Weston, Alison J.; Math, Vidya; Sanchez, Cesar; Leadlay, Peter F.; Mendez, Carmen; Salas, Jose A.; Zhang, Ming Q.
 CORPORATE SOURCE: Biotica Technol Ltd, Nat Prod Chem, Saffron Walden CB10 1XL, Essex, UK
 barrie.wilkinson@biotica.co.uk; steven.moss@biotica.co.uk
 SOURCE: Abstracts of Papers American Chemical Society, (AUG 22 2004) Vol. 228, No. Part 2, pp. U165.
 Meeting Info.: Meeting of the Division of Chemical Toxicology of the American-Chemical-Society held at the 228th National Meeting of the American-Chemical-Society. Philadelphia, PA, USA. August 22 -26, 2004. Amer Chem Soc, Div Chem Toxicol.
 CODEN: ACSRAL. ISSN: 0065-7727.
 DOCUMENT TYPE: Conference; (Meeting)

10/534210

Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jan 2006
Last Updated on STN: 25 Jan 2006
CC General biology - Symposia, transactions and proceedings 00520
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Pharmacology - General 22002
Pharmacology - Cardiovascular system 22010
Physiology and biochemistry of bacteria 31000
Food microbiology - General and miscellaneous 39008
IT Major Concepts
Pharmacology; Cardiovascular System (Transport and Circulation);
Bioprocess Engineering
IT Parts, Structures, & Systems of Organisms
aorta: circulatory system
IT Chemicals & Biochemicals
borrelidin: cardiovascular-drug, biosynthesis
IT Miscellaneous Descriptors
drug synthesis
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
Rodents, Vertebrates
ORGN Classifier
Streptomycetes and Related Genera 08840
Super Taxa
Actinomycetes and Related Organisms; Eubacteria; Bacteria;
Microorganisms
Organism Name
Streptomyces parvulus (species): expression system
Taxa Notes
Bacteria, Eubacteria, Microorganisms
RN 7184-60-3 (borrelidin)

L45 ANSWER 34 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 2004-36621 DRUGU C Full-text
TITLE: Stereoselective total synthesis of (-)-borrelidin.
AUTHOR: Vong B G; Kimm S H; Abraham S; Theodorakis E A
CORPORATE SOURCE: Univ.California
LOCATION: San Diego, Cal., USA
SOURCE: Angew.Chem.Int.Ed.Engl. (43, No. 30, 3947-51, 2004) 32 Ref.
CODEN: ACIEAY ISSN: 0570-0833
AVAIL. OF DOC.: Department of Chemistry and Biochemistry, University of
California San Diego, 9500 Gilman Drive, MC: 0358, La Jolla,
CA 92093-0358, U.S.A. (E.A.T.). (e-mail:
etheodor@chem.ucsd.edu).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB A total synthesis of the antibiotic (-)-borrelidin (1) was reported. The developed synthetic route was distinguished by the construction of a strained enynone-containing macrocycle (2) and the regioselective introduction of a cyano group by implementing a novel molybdenum-catalyzed hydrostannation

reaction. Compound (1) was afforded in a yield of 88%. Spectroscopic and analytical data for (1) were in accord with reported values. The late installation of the nitrile unit in a fully functionalized macrocyclic scaffold paves the way for the preparation of analogs of (1) that could be used to evaluate structure-activity relationship data of (1).

L45 ANSWER 35 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN

ACCESSION NUMBER: 2003-14543 DRUGU C Full-text

TITLE: Enantioselective total synthesis of borrelidin.

AUTHOR: Duffey M O; LeTiran A; Morken J P

CORPORATE SOURCE: Univ.North-Carolina

LOCATION: Chapel Hill, N.C., USA

SOURCE: J.Am.Chem.Soc. (125, No. 6, 1458-59, 2003) 1 Fig. 24 Ref.

CODEN: JACSAT ISSN: 0002-7863

AVAIL. OF DOC.: Dept. Chemistry, Venable and Kenan Labs., University of North Carolina, Chapel Hill, NC 27599-3290, U.S.A. (email: morken@unc.edu). (J.P.M.).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The enantioselective total synthesis of the angiogenesis inhibitor borrelidin (1) is described, starting with reductive aldol coupling of methyl acrylate and p-methoxybenzyloxyacetaldehyde. Iridium indanepybox-catalyzed enantioselective reductive aldol reaction established the stereogenic centers at C3, C4, C10 and C11. The method involved large scale asymmetric reductive aldol reactions and methods to reverse the usual regioselection in hydrostannylation of propargyl alcohols. The method allowed for late stage derivatization of the cyanodiene core, which may allow discovery of nontoxic analogs of the natural product.

L45 ANSWER 36 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN

ACCESSION NUMBER: 2004-03117 DRUGU M Full-text

TITLE: In-vitro and in vivo antimalarial activities of a non-glycosidic 18-membered macrolide antibiotic, borrelidin, against drug-resistant strain of Plasmodia.

AUTHOR: Otoguro K; Ui H; Ishiyama A; Kobayashi M; Togashi H; Tokahashi Y; Masuma R; Tanaka H; Tomoda H; Omura S

CORPORATE SOURCE: Univ.Kitasato

LOCATION: Tokyo, Japan

SOURCE: J.Antibiot. (56, No. 8, 727-29, 2003) 1 Fig. 3 Tab. 14 Ref.

CODEN: JANTAJ ISSN: 0021-8820

AVAIL. OF DOC.: Kitasato Institute for Life Sciences, Kitasato University, 5-9-1 Shirokane, Minato-ku, Tokyo 108- 8642, Japan. (S.O.). (11 Authors).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The in vivo and in vitro antimalarial activity of borrelidin (BO), isolated from the cultured broth of an actinomycete strain OM-0060, is reported. BO showed more potent in vitro activity vs. the drug-resistant K1 strain of Plasmodium falciparum than the clinically used artemether, artesunate and chloroquine and showed similar activity vs. the drug-sensitive FCR3 strain of P. falciparum to artemether and artesunate and was more potent than chloroquine. BO displayed relatively low cytotoxicity vs. MCR5 cells. BO had in vivo (s.c.) antimalarial activity vs. both rodent malaria-derived P. berghei and P. yoelii and was more effective than artemether, artesunate and

chloroquine vs. the chloroquine-resistant strain (*P. yoelii*). BO also showed more potent p.o. activity than artemether, artesunate and chloroquine.

L45 ANSWER 37 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
 ACCESSION NUMBER: 2003-00062 DRUGU C Full-text
 TITLE: Progress toward the total synthesis of borrelidin.
 AUTHOR: Duffey M O; LeTiran A; Morken J P
 CORPORATE SOURCE: Univ.North-Carolina
 LOCATION: Chapel Hill, N.C., USA
 SOURCE: Abstr.Pap.Am.Chem.Soc. (224 Meet., Pt. 2, ORGN 427, 2002)
 CODEN: ACSRAL ISSN: 0065-7727
 AVAIL. OF DOC.: Department of Chemistry, University of North Carolina, CB#
 3290 Venable Hall, Chapel Hill, NC 27514, U.S.A. (e-mail:
 mduffey@email.unc.edu).
 LANGUAGE: English
 DOCUMENT TYPE: Journal
 FIELD AVAIL.: AB; LA; CT
 FILE SEGMENT: Literature

AB A total synthesis of the antibiotic borrelidin was presented. The strategy for the synthesis of borrelidin focused on the use of an iridium-indanepybox catalyzed enantioselective reductive aldol reaction to establish the stereogenic centers at C-8, C-9, C-15, and C-16. The Authors also sought to develop a protocol for the construction of the challenging acrylonitrile moiety at C-7. In order to accomplish these goals a retrosynthetic approach involving the synthesis of two main fragments, alkyne (1) and vinyl iodide (2), to produce the core structure of borrelidin, was envisioned. The synthesis of (1-2) was reported. (conference abstract: 224th ACS National Meeting, Boston, Massachusetts, USA, 2002).

L45 ANSWER 38 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
 ACCESSION NUMBER: 2001-09193 DRUGU B P Full-text
 TITLE: Borrelidin inhibits a cyclin-dependent kinase (CDK),
 Cdc28/Cln2, of *Saccharomyces cerevisiae*.
 AUTHOR: Tsuchiya E; Yukawa M; Miyakawa T; Kimura K I; Takahashi H
 CORPORATE SOURCE: Univ.Hiroshima; Snow-Brand-Milk-Products
 LOCATION: Hiroshima; Tochigi, Jap.
 SOURCE: J.Antibiot. (54, No. 1, 84-90, 2001) 5 Fig. 21 Ref.
 CODEN: JANTAJ ISSN: 0021-8820
 AVAIL. OF DOC.: Department of Molecular Biotechnology, Graduate School of
 Advanced Sciences of Matter, Hiroshima University,
 Higashi-Hiroshima 739-8527, Japan. (e-mail:
 stsuchi@hiroshima-u.ac.jp).
 LANGUAGE: English
 DOCUMENT TYPE: Journal
 FIELD AVAIL.: AB; LA; CT
 FILE SEGMENT: Literature

AB Borrelidin was identified as an inhibitor of cyclin-dependent kinase (CDK) of the budding yeast *Sacch. cerevisiae* Cdc28/Cln2. Borrelidin was shown to arrest both haploid and diploid cells in G1 phase at the point indistinguishable from that of alpha-mating pheromone, at concentrations that did not affect the gross protein synthesis. Results suggest that borrelidin may be a useful lead in the development of new CDK inhibitors of higher eukaryotes.

L45 ANSWER 39 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
 ACCESSION NUMBER: 3199 DRUGU
 FILE SEGMENT: Registry

10/534210

DERWENT DRUG REGISTRY NAME: BORRELIDI
DERWENT DRUG NAME: BORRELIDIN
CAS REGISTRY NUMBER: 7184-60-3
CONTROLLED TERM: ANTIBIOTICS
SUBSTRUCTURE TERM: MACROCYCLE; CYCLOPENTANE; LACTONE; POLYOLEFIN;
POLYALCOHOL HYDROXYACID; NITRILE;
OXACYCLOOCTADECANE; AH-LINKED-CC
MULTIPUNCH CODE: 02& *G; 02- *G; 04& *G; 047 *G; 06& *G; 068 *G; 075
*G; 078 *G; 091 *G; 094 *G; 10- *G; 103 *G; 105 *G;
106 *G; 108 *G; 109 *G; 12& *G; 12- *G; 13& *G; 134
*G; 164 *G; 17- *G; 176 *G; 18- *G; 182 *G; 232 *G;
237 *G; 254 *G; 257 *G

L45 ANSWER 40 OF 40 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1974191119 EMBASE Full-text
TITLE: Alteration of structure or level of threonyl tRNA synthetase in borrelidin resistant mutants of E. coli.
AUTHOR: Nass, G.; Thomale, J.
CORPORATE SOURCE: Abt. Molek. Biol., Max Planck Inst. Exp. Med., Gottingen, Germany.
SOURCE: FEBS Letters, (1974) Vol. 39, No. 2, pp. 182-186.
ISSN: 0014-5793 CODEN: FEBLAL
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
029 Clinical and Experimental Biochemistry
LANGUAGE: English

AB Borrelidin inhibits the growth of E. coli effectively. Since no other biochemical reaction is known to be attacked directly by Borrelidin than the enzymatic activity of the threonyl-t RNA synthetase (ThRS), Borrelidin resistant mutants of E. coli K12 and E. coli B were isolated with the aim of finding mutants with an altered structure or level of ThRS. The ThRS of 15 Borrelidin resistant mutants of each E. coli strain was investigated. The characterization of the ThRS of some Borrelidin resistant mutants is described. By means of determination of enzyme constants and antibody neutralization curves it is shown that the Borrelidin resistant mutants can be divided into 3 groups: one group of mutants exhibits constitutively increased levels of wildtype ThRS, the second group structurally altered ThRS, and in a third group of mutants no alteration of the structure or level of ThRS could be detected. This suggests that Borrelidin resistance in the latter mutants is due to some other reason than alteration of ThRS activity. Since it is known that the ThRS participates in the regulation of formation of the threonine biosynthetic enzymes, the level of aspartokinase was also determined in the Borrelidin resistant mutants grown in the presence and absence of Borrelidin.

CT Medical Descriptors:

*escherichia coli
in vitro study
microorganism
*mutant
theoretical study

CT Drug Descriptors:

*borrelidin
*threonine transfer rna ligase

RN (borrelidin) 7184-60-3; (threonine transfer RNA ligase)
9023-46-5

10/534210

***** SEARCH HISTORY *****

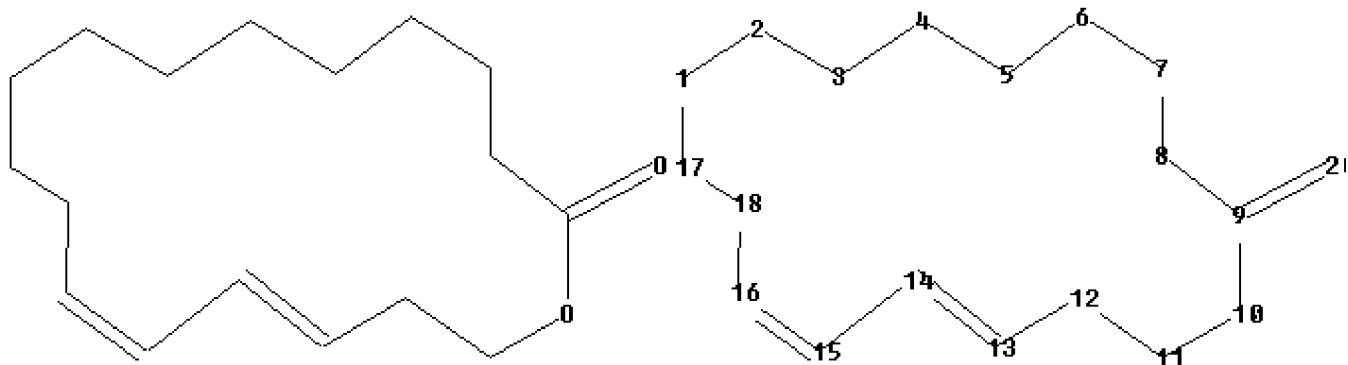
=> d his nofile

(FILE 'HOME' ENTERED AT 08:14:53 ON 04 SEP 2008)

FILE 'HCAPLUS' ENTERED AT 08:15:16 ON 04 SEP 2008

L1 1 SEA ABB=ON PLU=ON US20070065920/PN
D IBIB AB IT SC
L2 SCR 2043 OR 1918
L3 STRUCTURE UPLOADED
D

Uploading L11.str



chain nodes :

20

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

chain bonds :

9-20

ring bonds :

1-2 1-17 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-12 12-13 13-14 14-15

15-16 16-18 17-18

exact/norm bonds :

9-20

exact bonds :

1-2 1-17 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-12 12-13 13-14 14-15

15-16 16-18 17-18

isolated ring systems :

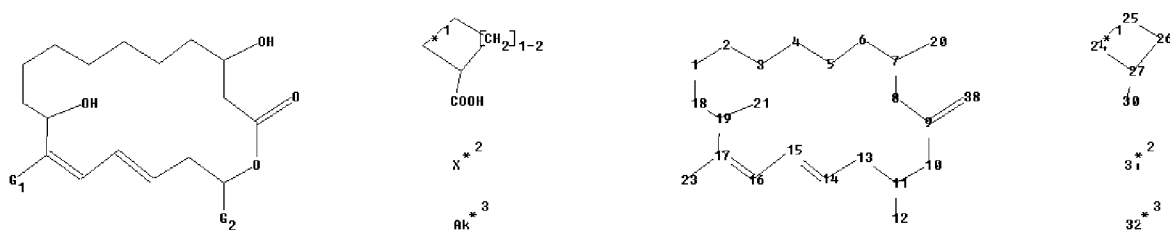
containing 1 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 20:CLASS

L4 2 SEA SSS SAM L3 NOT L2
L5 68 SEA SSS FUL L3 NOT L2
SAVE TEMP L5 KAM240REGL11/A
L6 STRUCTURE UPLOADED
D

Uploading L12.str



```

chain nodes :
12 20 21 23 30 31 32 38
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 13 14 15 16 17 18 19 24 25 26 27
chain bonds :
7-20 9-38 11-12 17-23 19-21 27-30
ring bonds :
1-2 1-18 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-13 13-14 14-15 15-16
16-17 17-19 18-19 24-25 24-27 25-26 26-27
exact/norm bonds :
7-20 9-38 11-12 17-23 19-21
exact bonds :
1-2 1-18 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-13 13-14 14-15 15-16
16-17 17-19 18-19 24-25 24-27 25-26 26-27 27-30
isolated ring systems :
containing 1 : 24 :

```

G1:CH3,COOH,CN

G2:[*1],[*2],[*3]

Match level :

```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:CLASS 21:CLASS
23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom 30:CLASS 31:CLASS 32:CLASS
38:CLASS

```

L7 0 SEA SUB=L5 SSS SAM L6

FILE 'HCAPLUS' ENTERED AT 08:44:11 ON 04 SEP 2008

L8 86 SEA ABB=ON PLU=ON L5

FILE 'REGISTRY' ENTERED AT 08:44:27 ON 04 SEP 2008

L9 17 SEA SUB=L5 SSS FUL L6

FILE 'HCAPLUS' ENTERED AT 08:44:57 ON 04 SEP 2008

L10 86 SEA ABB=ON PLU=ON L9

10/534210

FILE 'REGISTRY' ENTERED AT 08:45:56 ON 04 SEP 2008
SAVE TEMP L9 KAM240REGL12/A

FILE 'HCAPLUS' ENTERED AT 08:47:16 ON 04 SEP 2008

L11 14 SEA ABB=ON PLU=ON L10 AND 3/SC,SX
L12 5382 SEA ABB=ON PLU=ON BIOSYNTHET? GENE#
L13 4 SEA ABB=ON PLU=ON L10 AND L12
L14 5465 SEA ABB=ON PLU=ON POLYKETID?
L15 6 SEA ABB=ON PLU=ON L10 AND L14
L16 18 SEA ABB=ON PLU=ON L11 OR L13 OR L15
L17 19 SEA ABB=ON PLU=ON L10 AND PHARMAC?/SC,SX
L18 33 SEA ABB=ON PLU=ON L16 OR L17
L19 36472 SEA ABB=ON PLU=ON BIOSYNTHET?
L20 9 SEA ABB=ON PLU=ON L10 AND L19
L21 37 SEA ABB=ON PLU=ON L18 OR L20
L22 478 SEA ABB=ON PLU=ON SALAS J?/AU
L23 305 SEA ABB=ON PLU=ON MENDEZ C?/AU
L24 51 SEA ABB=ON PLU=ON OLANO C?/AU
L25 3325 SEA ABB=ON PLU=ON SANCHEZ C?/AU
L26 100 SEA ABB=ON PLU=ON BRANA A?/AU
L27 449 SEA ABB=ON PLU=ON WILKINSON B?/AU
L28 5002 SEA ABB=ON PLU=ON MARTIN C?/AU
L29 1074 SEA ABB=ON PLU=ON MOSS S?/AU
L30 197 SEA ABB=ON PLU=ON LEADLAY P?/AU
L31 16 SEA ABB=ON PLU=ON OLIYNYK M?/AU

FILE 'REGISTRY' ENTERED AT 08:57:10 ON 04 SEP 2008

L32 1 SEA ABB=ON PLU=ON L9 AND (MEDLINE OR BIOSIS OR DRUGU OR
EMBASE)/LC

FILE 'MEDLINE' ENTERED AT 08:57:41 ON 04 SEP 2008

L33 31 SEA ABB=ON PLU=ON L32
L34 3 SEA ABB=ON PLU=ON L33 AND BIOSYNTHET?
D TI KWIC 1-3

FILE 'BIOSIS' ENTERED AT 08:58:27 ON 04 SEP 2008

L35 63 SEA ABB=ON PLU=ON L32
L36 6 SEA ABB=ON PLU=ON L33 AND BIOSYNTHET?

FILE 'DRUGU' ENTERED AT 08:58:53 ON 04 SEP 2008

L37 0 SEA ABB=ON PLU=ON L33 AND BIOSYNTHET?
L38 8 SEA ABB=ON PLU=ON L32
D SCAN
D TI KWIC 1-4

FILE 'EMBASE' ENTERED AT 08:59:36 ON 04 SEP 2008

L39 3 SEA ABB=ON PLU=ON L33 AND BIOSYNTHET?

FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 09:00:06 ON 04 SEP 2008

L40 176 SEA ABB=ON PLU=ON ((L22 OR L23 OR L24 OR L25 OR L26 OR L27
OR L28 OR L29 OR L30 OR L31)) AND BIOSYNTHET? GENE#
L41 6 SEA ABB=ON PLU=ON L40 AND BORRELIDIN
SAVE TEMP L41 KAM240MULTIN/A

FILE 'HCAPLUS' ENTERED AT 09:04:34 ON 04 SEP 2008

L42 7 SEA ABB=ON PLU=ON (((L22 OR L23 OR L24 OR L25 OR L26 OR L27
OR L28 OR L29 OR L30 OR L31)) AND L10) OR (L1 AND L10)
L43 30 SEA ABB=ON PLU=ON L21 NOT L42
SAVE TEMP L42 KAM240HCAIN/A

10/534210

SAVE TEMP L43 KAM240HCAP/A

FILE 'STNGUIDE' ENTERED AT 09:06:18 ON 04 SEP 2008

D QUE L42

D QUE L41

FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 09:10:22 ON 04 SEP 2008

L44 8 DUP REM L42 L41 (5 DUPLICATES REMOVED)

ANSWERS '1-7' FROM FILE HCAPLUS

ANSWER '8' FROM FILE BIOSIS

D L44 1-7 IBIB ABS HITSTR

D L44 8 IBIB AB

D QUE L43

D QUE L34

D QUE L36

D QUE L38

D QUE L39

FILE 'HCAPLUS, MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 09:11:54 ON 04
SEP 2008

L45 40 DUP REM L43 L34 L36 L38 L39 (10 DUPLICATES REMOVED)

ANSWERS '1-30' FROM FILE HCAPLUS

ANSWERS '31-32' FROM FILE MEDLINE

ANSWER '33' FROM FILE BIOSIS

ANSWERS '34-39' FROM FILE DRUGU

ANSWER '40' FROM FILE EMBASE

D L45 1-30 IBIB ABS FHITSTR HITIND

D L45 31-40 IBIB AB HITIND